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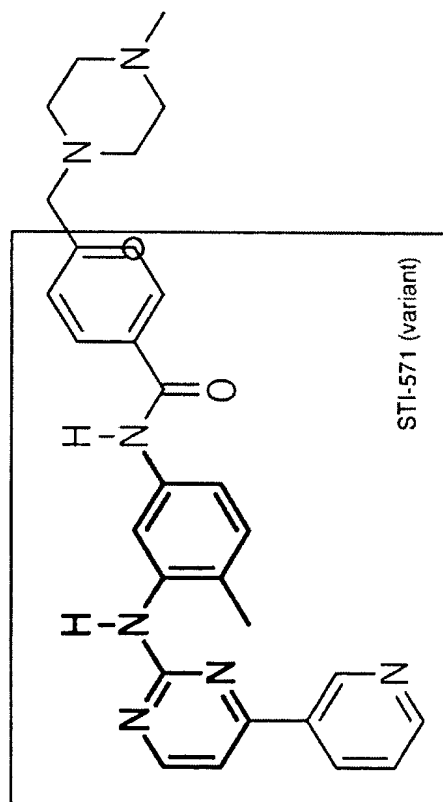
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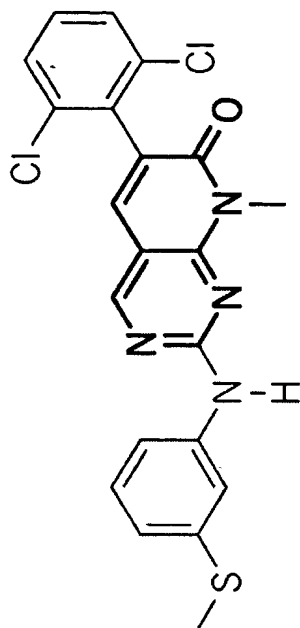
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STI-571 (variant)

STI-571



PD173955

Figure 1

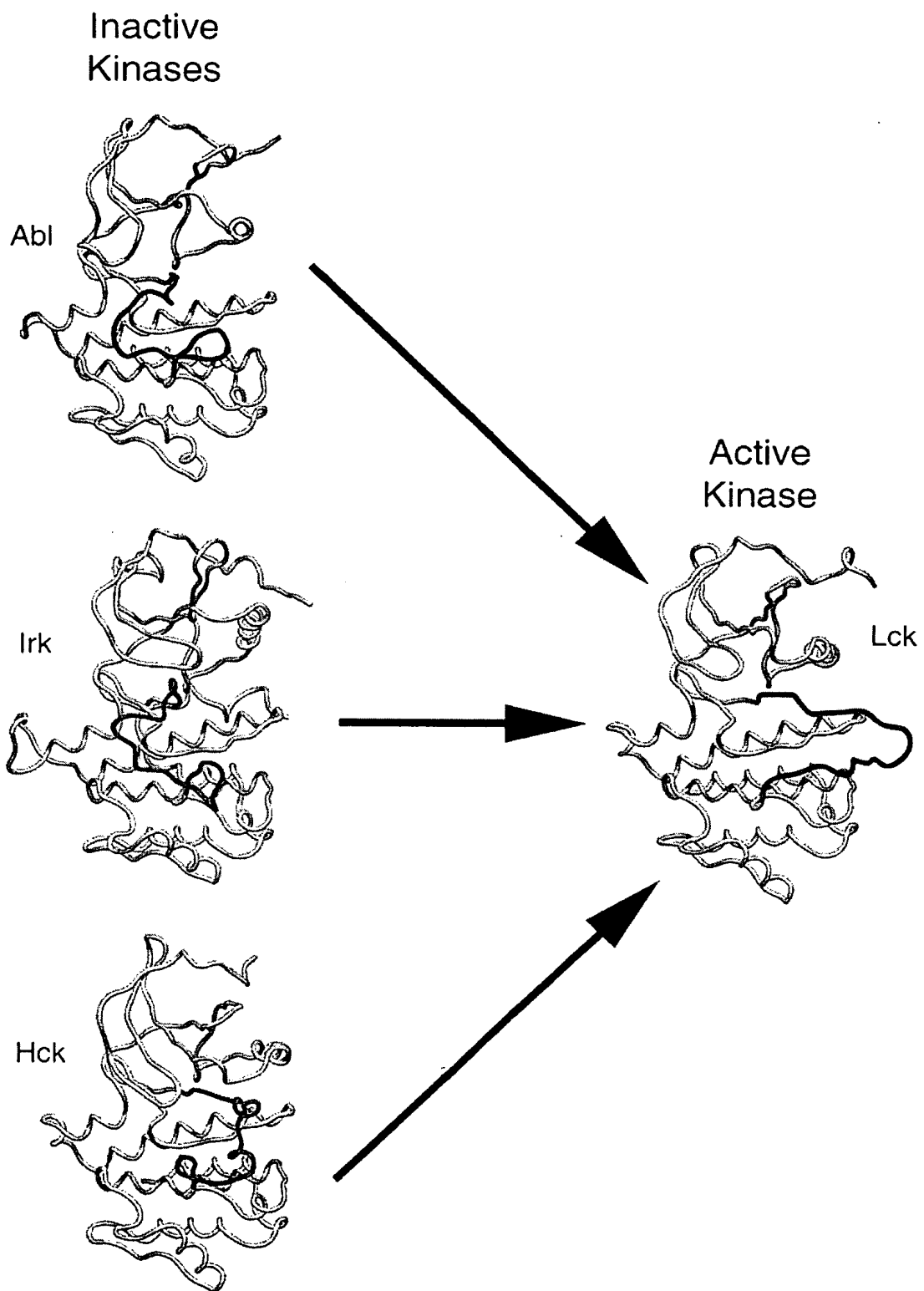
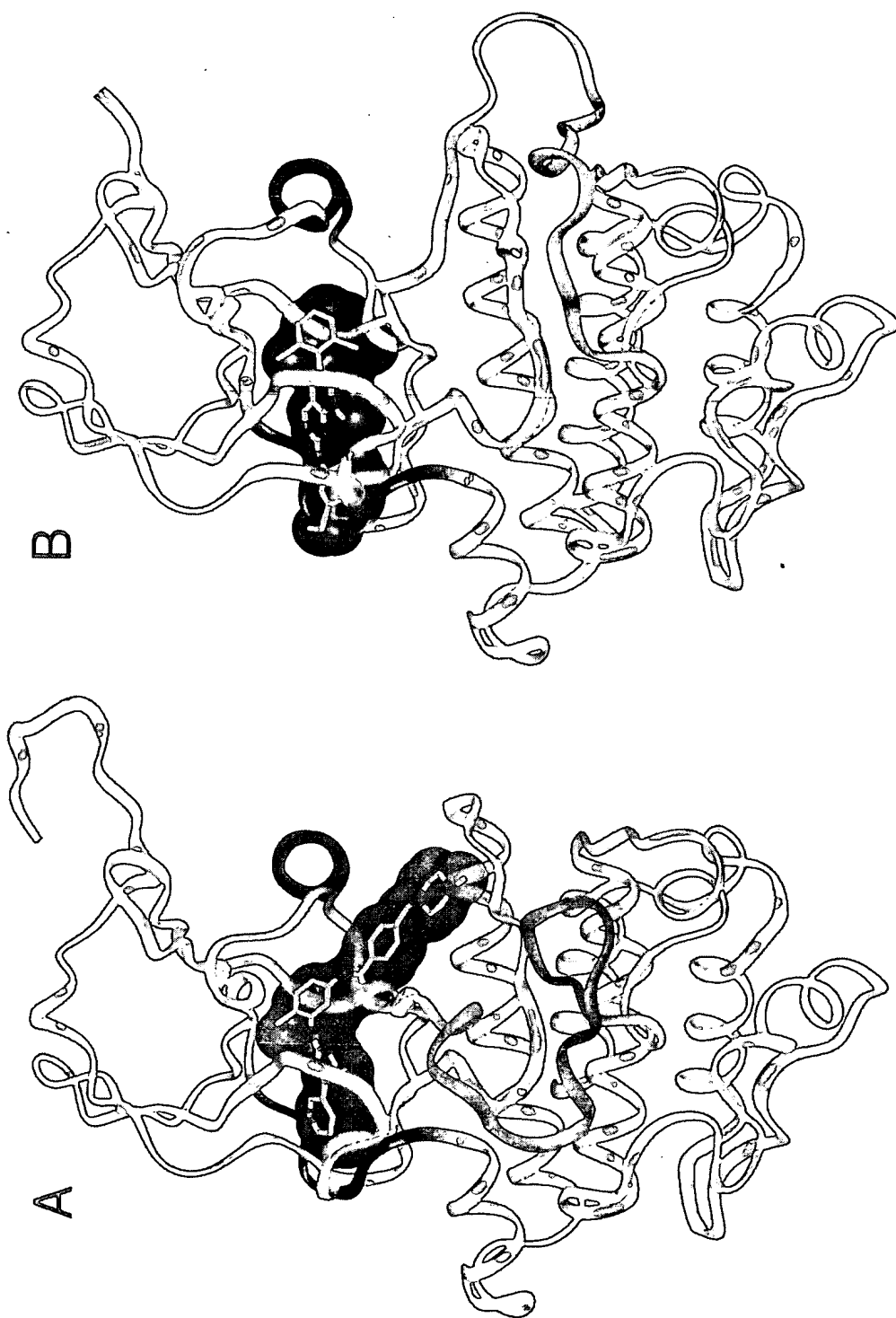
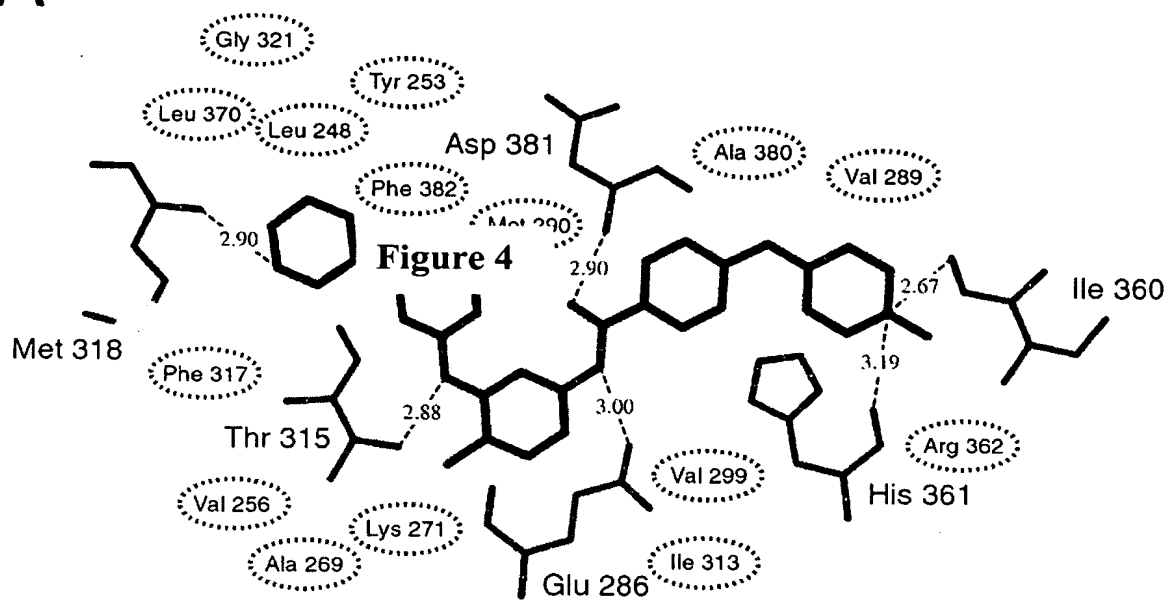


Figure 2



**Figure 3**

A



B

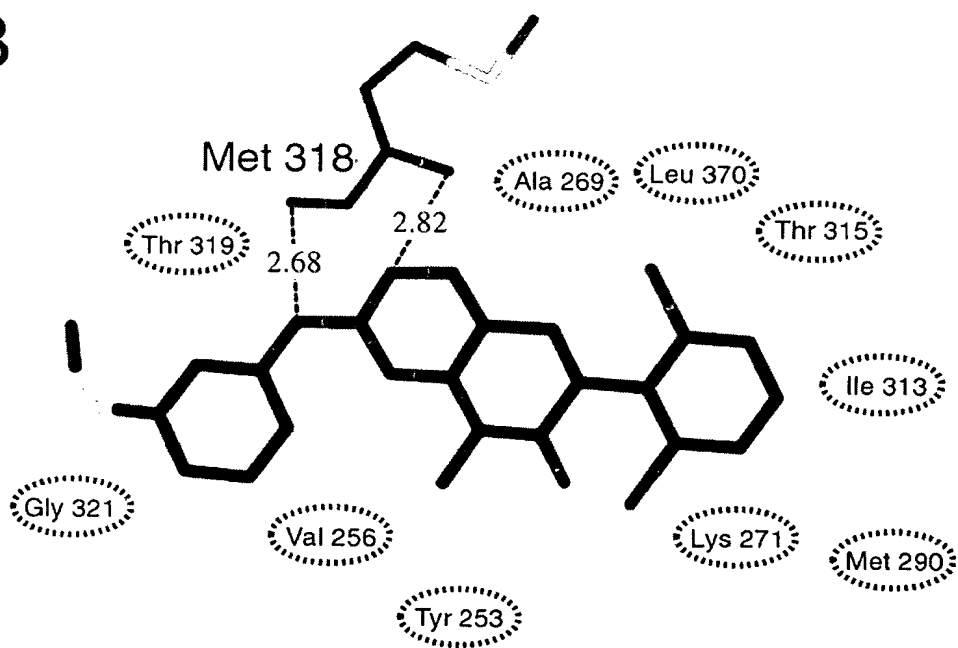
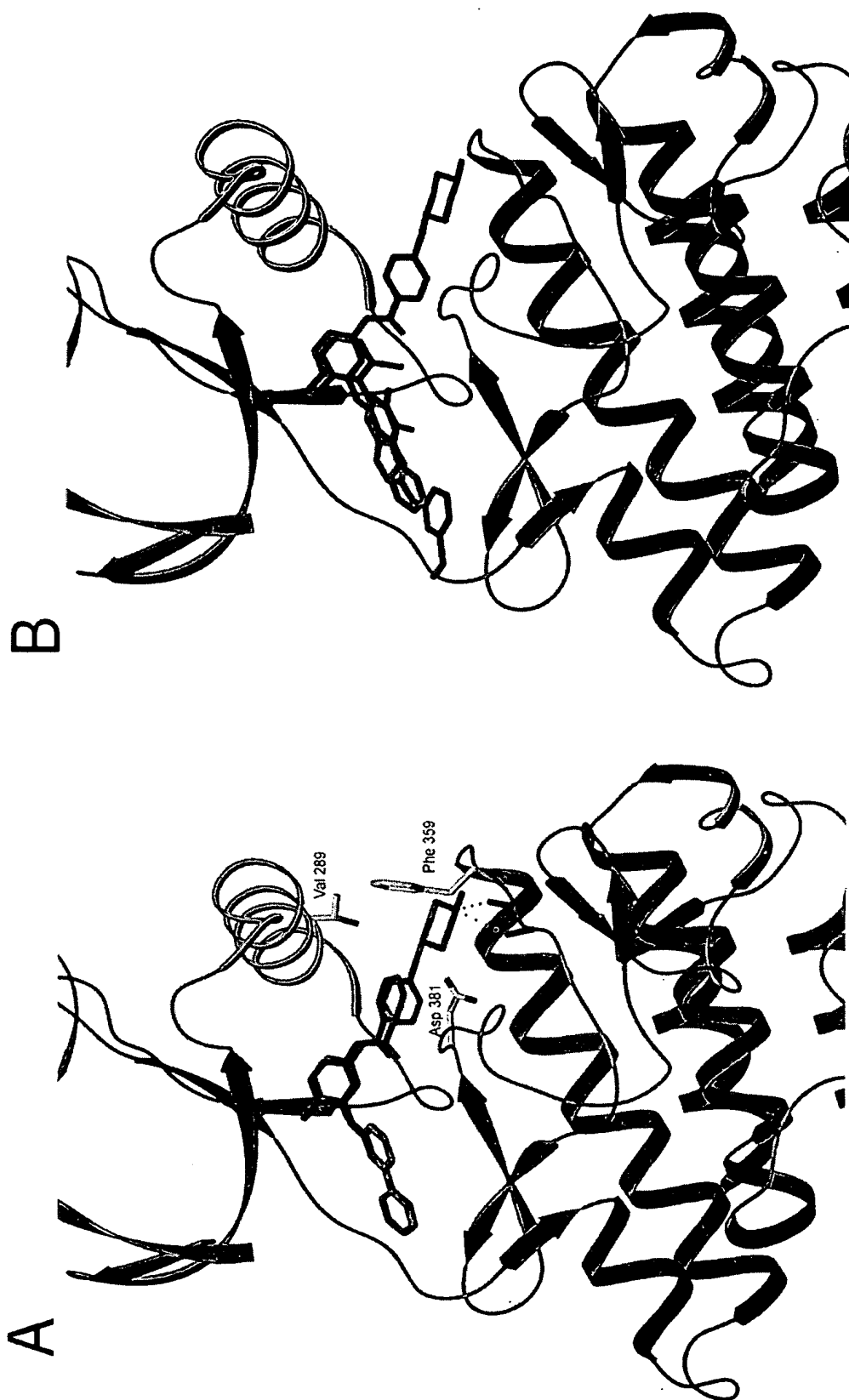
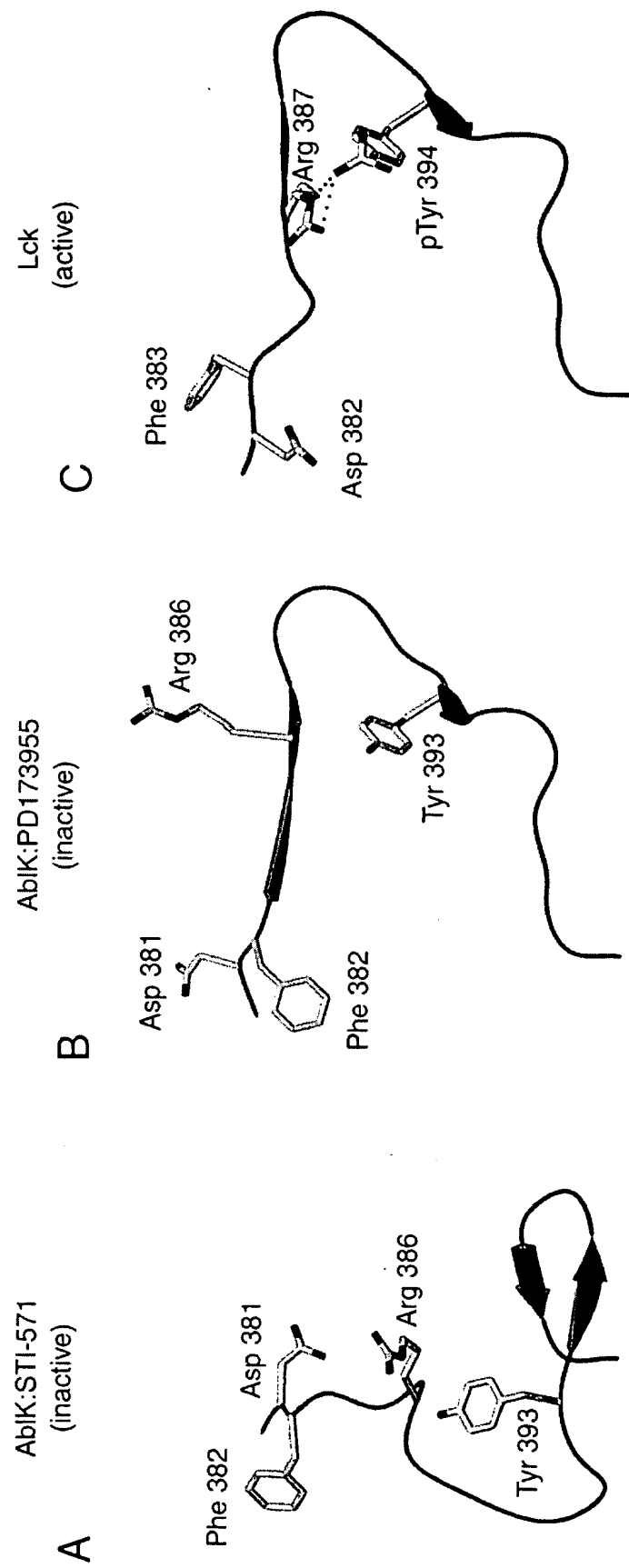


Figure 4



**Figure 5**

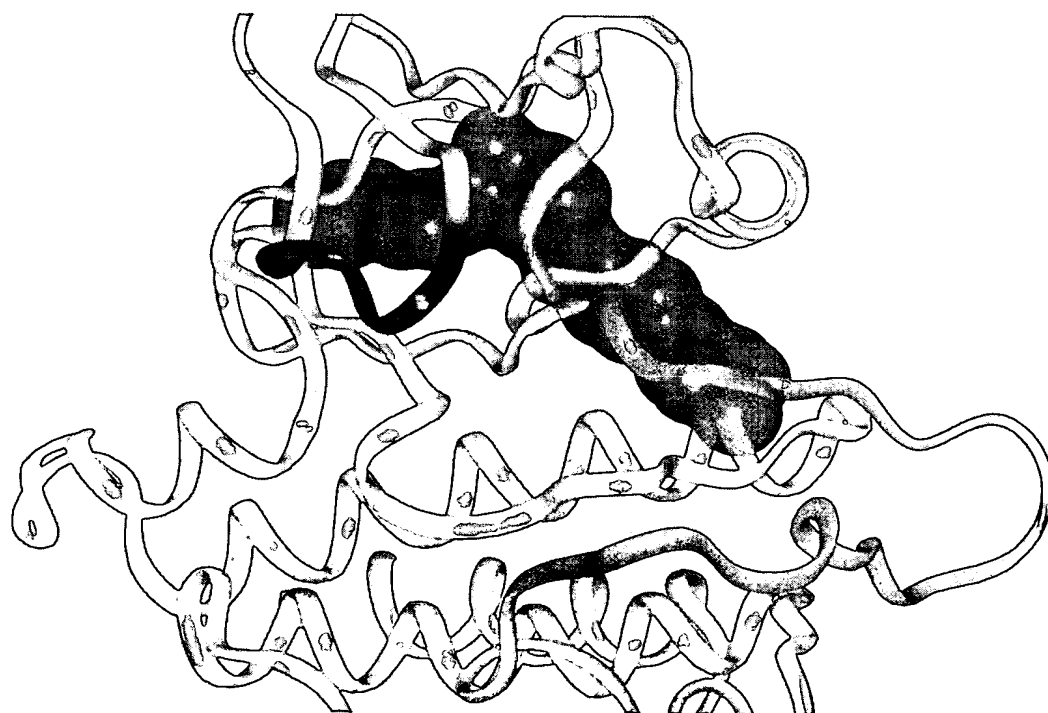


**Figure 6**

A



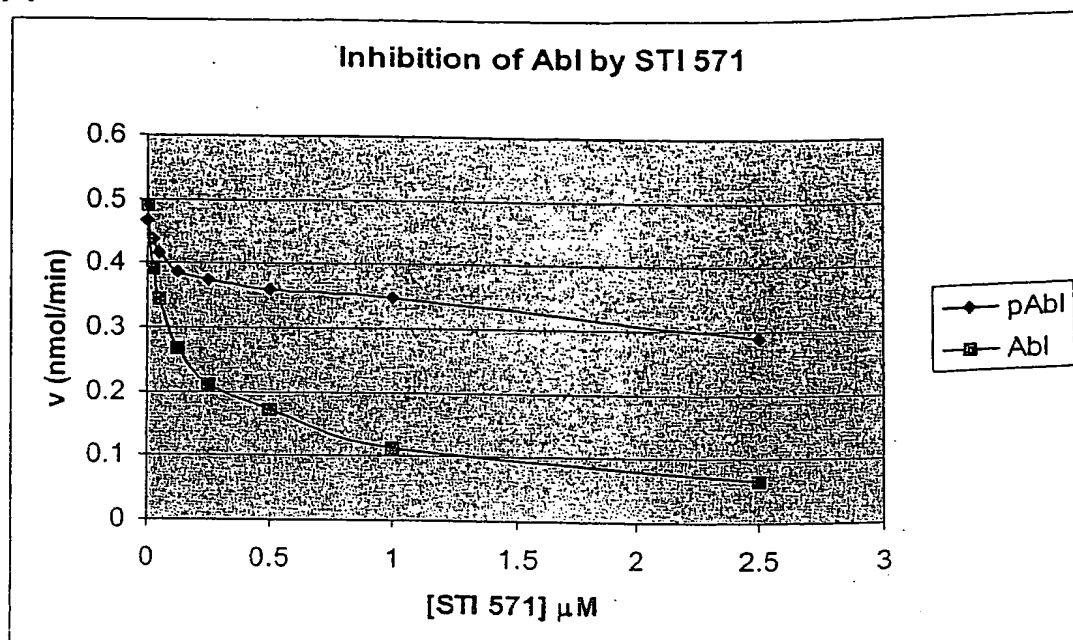
B



**Figure 7**



A



B

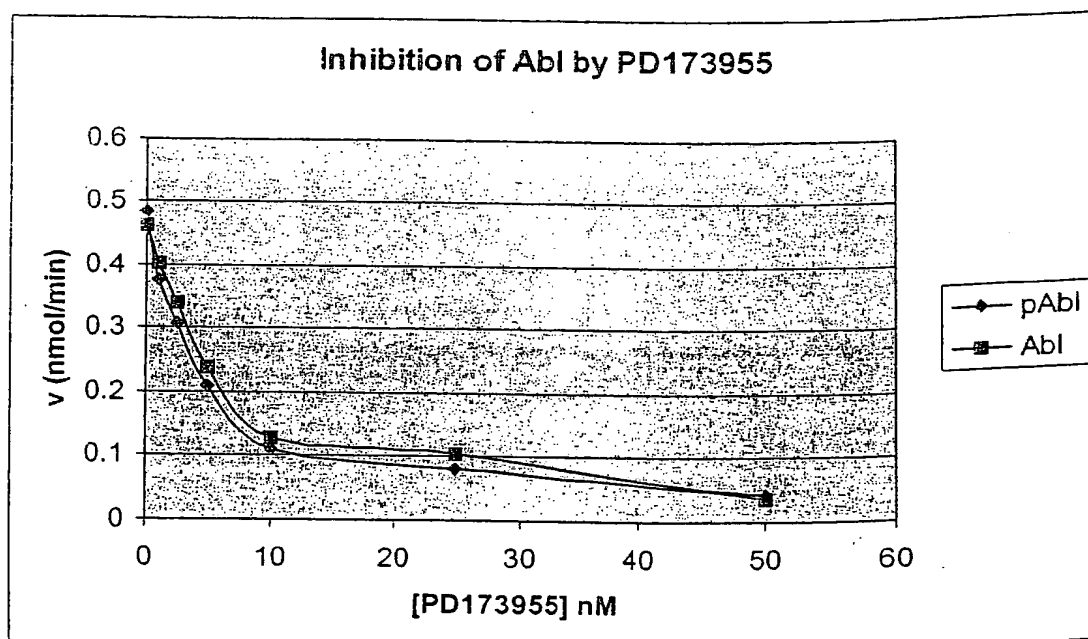
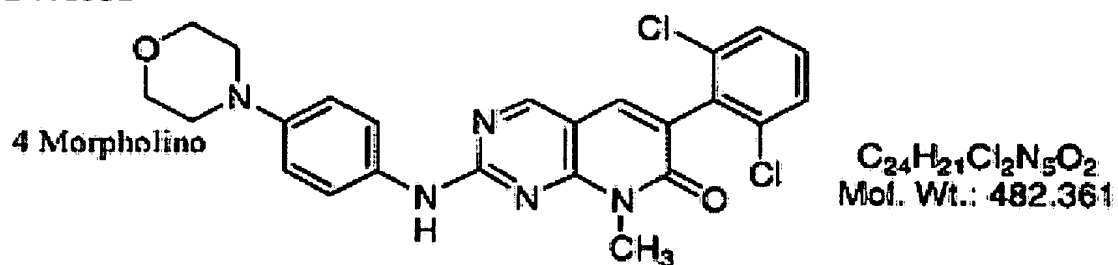
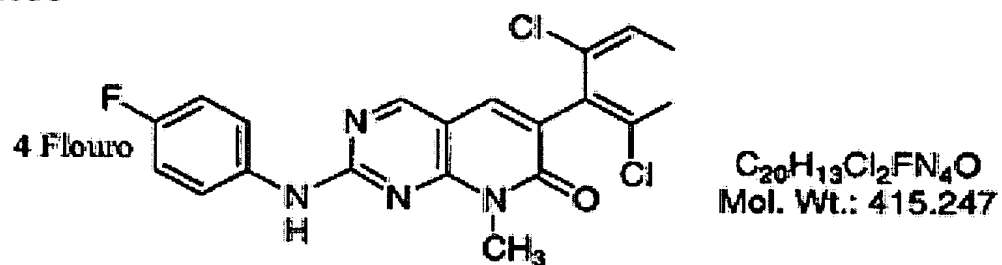


Figure 8

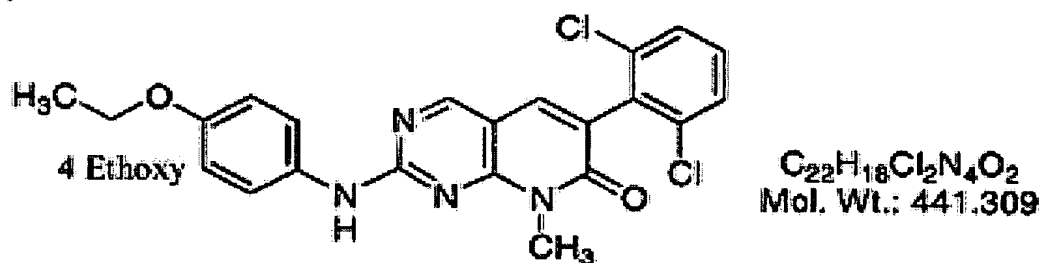
PD173952



PD173956



PD173958



PD166326

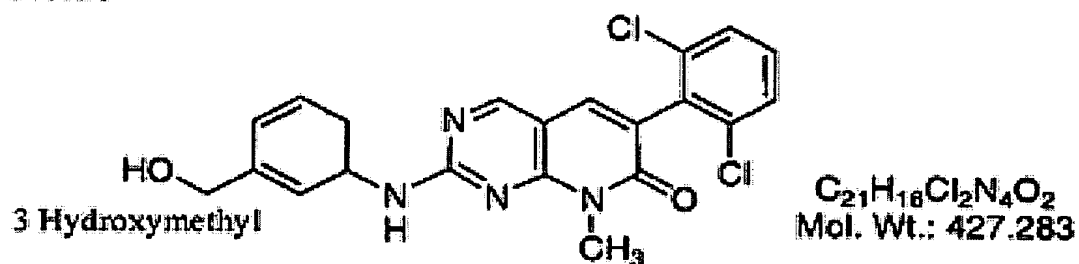
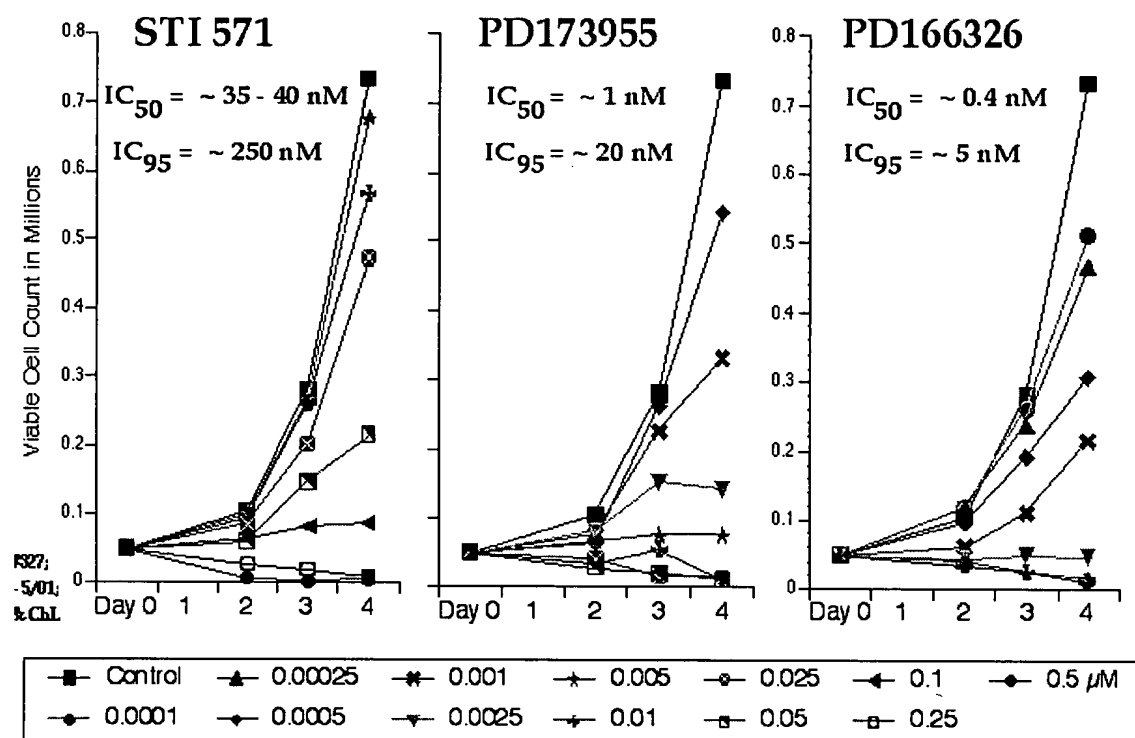


Figure 9

**Comparative Inhibition of Growth of R10 NEG Cells in Liquid Culture by STI571 (5 - 500 nM), PD173955 (0.5 - 50 nM), & PD166326 (0.1 - 10 nM)**



**Figure 10**

## Inhibition of $^3\text{H}$ -Tdr Uptake in Fresh Blast Cells from CML Patient in Blastic Phase by STI571, PD173955, & PD166326

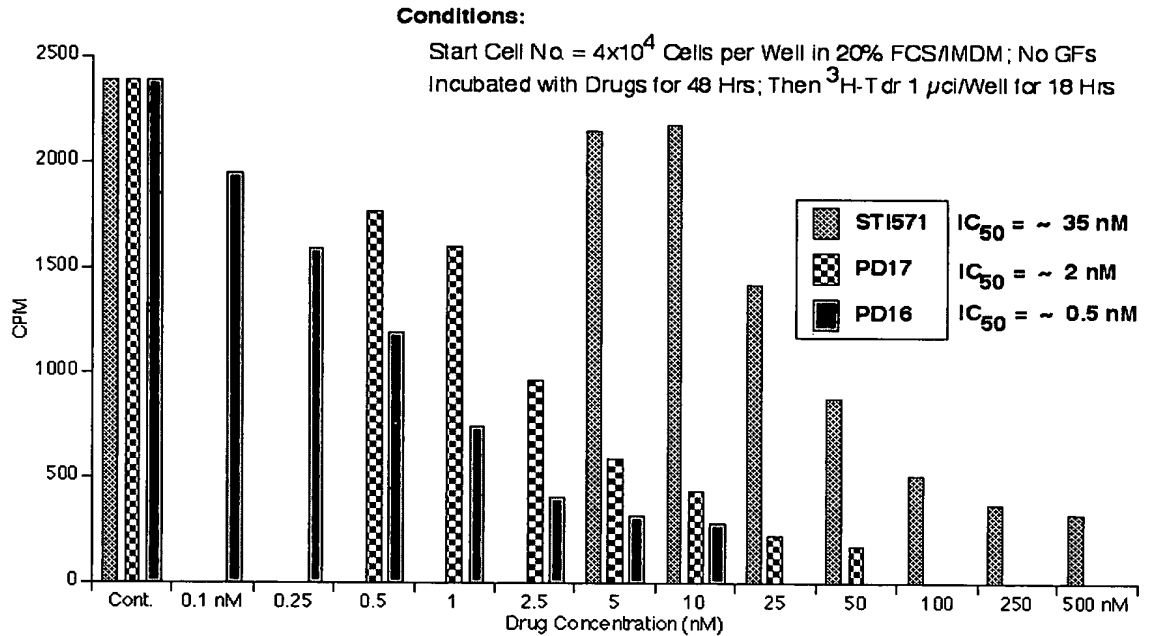


Figure 11

## Inhibition of $^3\text{H}$ -Tdr Uptake by Fresh Blast Cells with & without Cytokines from the Same CML Patient in Blastic Phase by STI571, PD173955, & PD166326

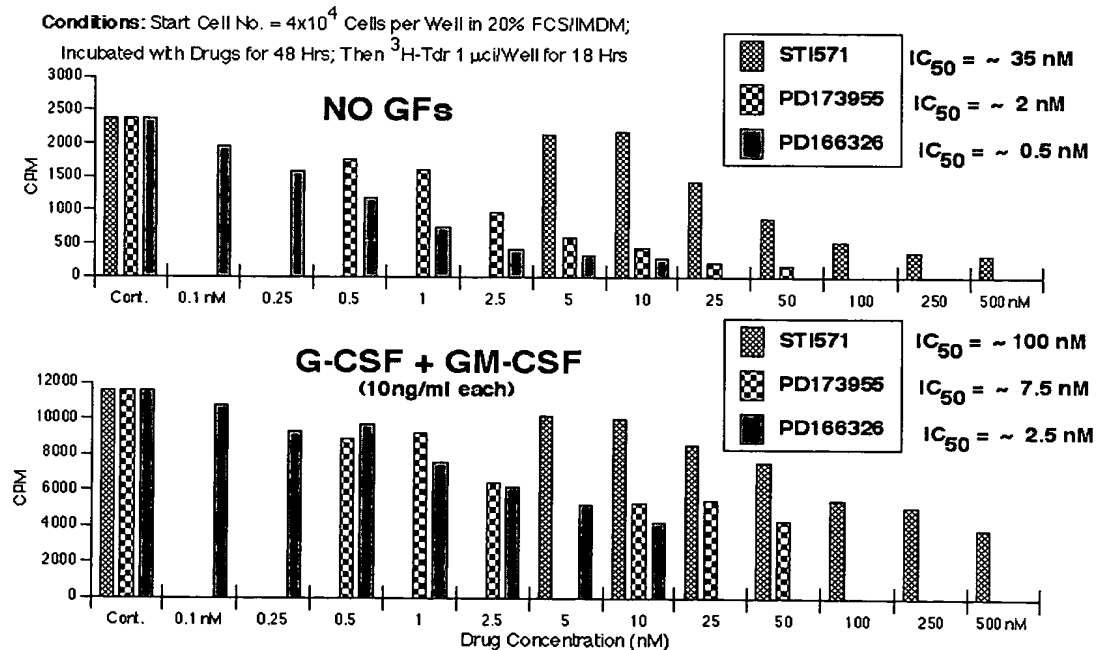


Figure 12

### Relative Sensitivity of Various Human Tumor Cell Lines to PD173955

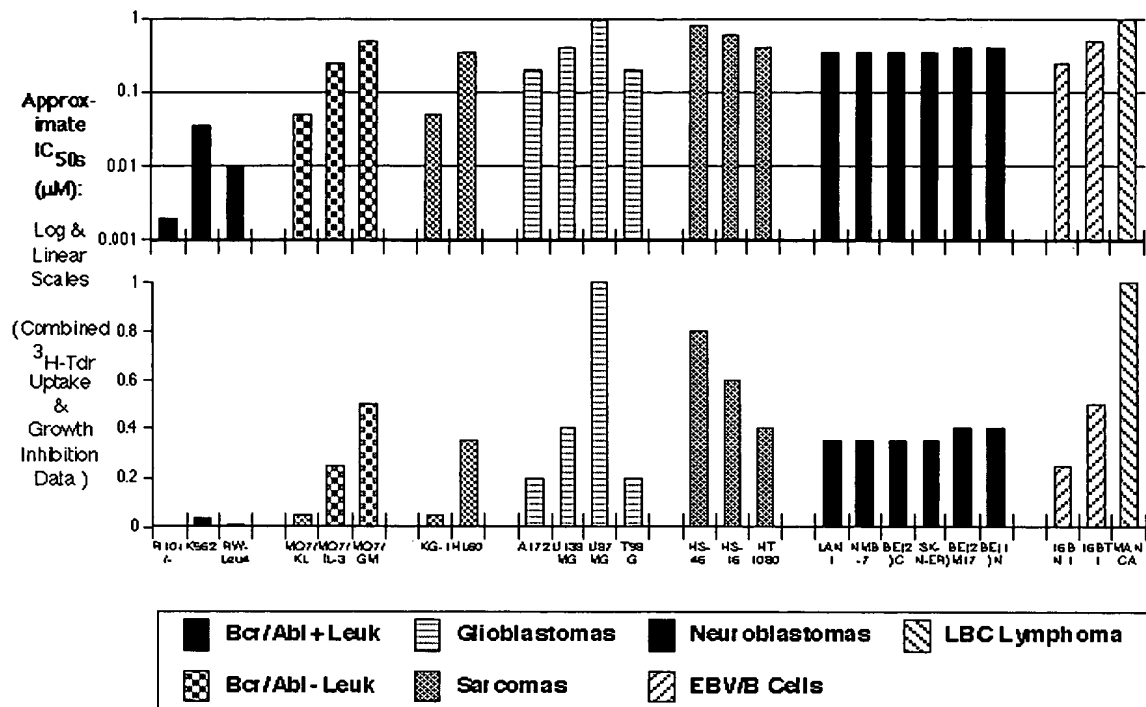


Figure 13

### Relative Sensitivity of Various Human Tumor Cell Lines to PD173955 & STI571

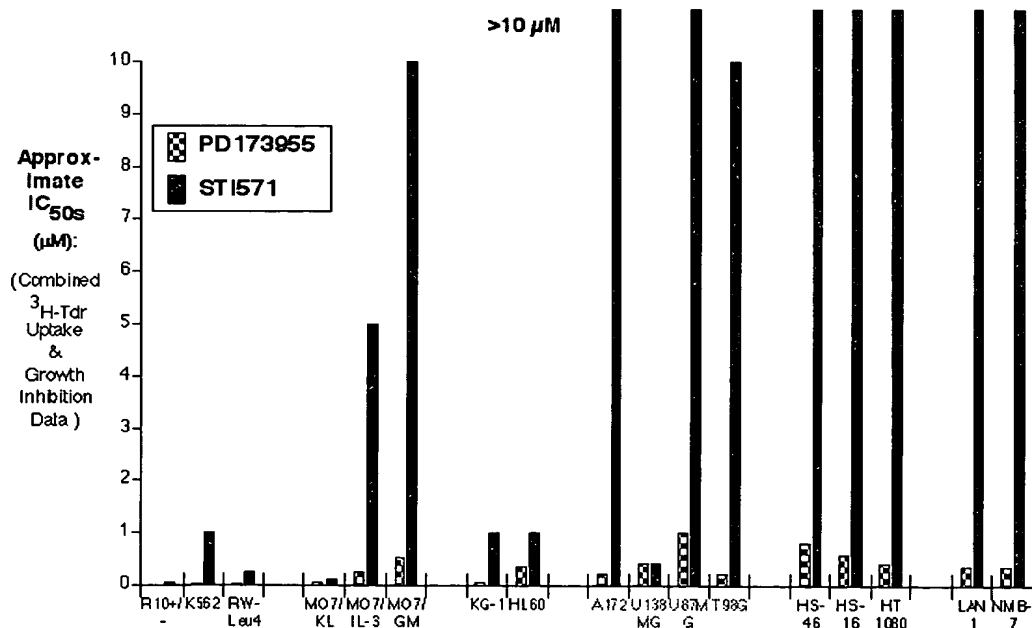


Figure 14

## PD 166326 binding to Abl Kinase (Modelled)

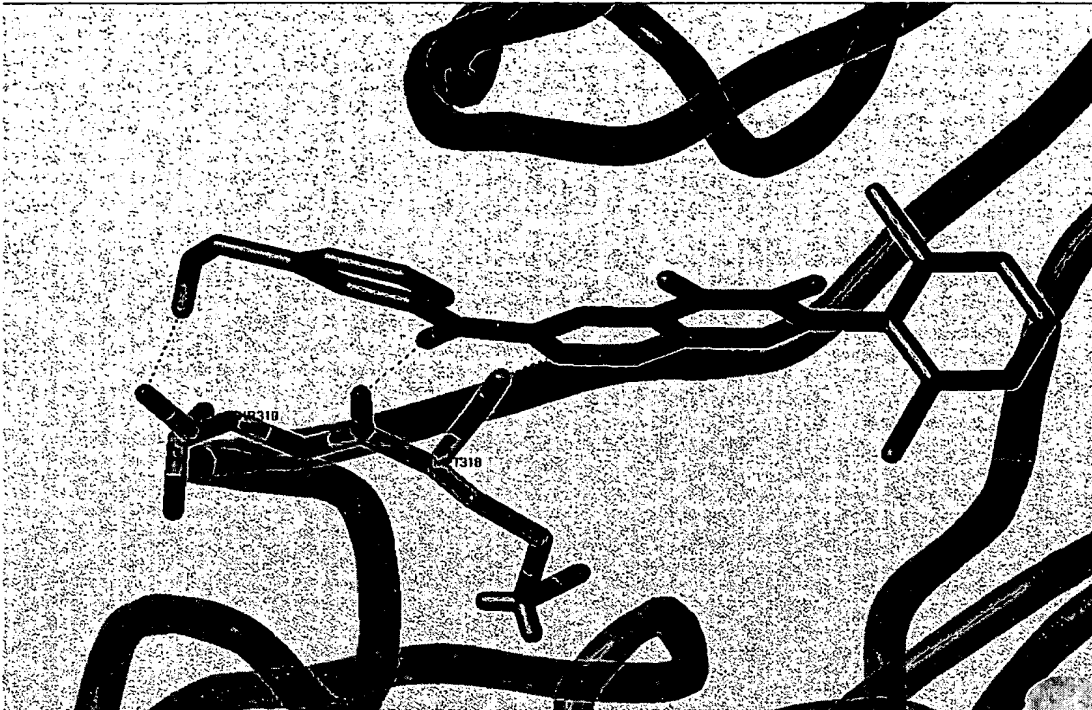


Figure 15

## 10 nM PD173955 Inhibits Primary Early CML CD34+ GM Progenitors (0 - 5 Days) Substantially More than Later Maturing Progenitors (4 - 8 Days); No Inhibition of Comparable Normal Progenitors (Mean Values 3 Experiments)

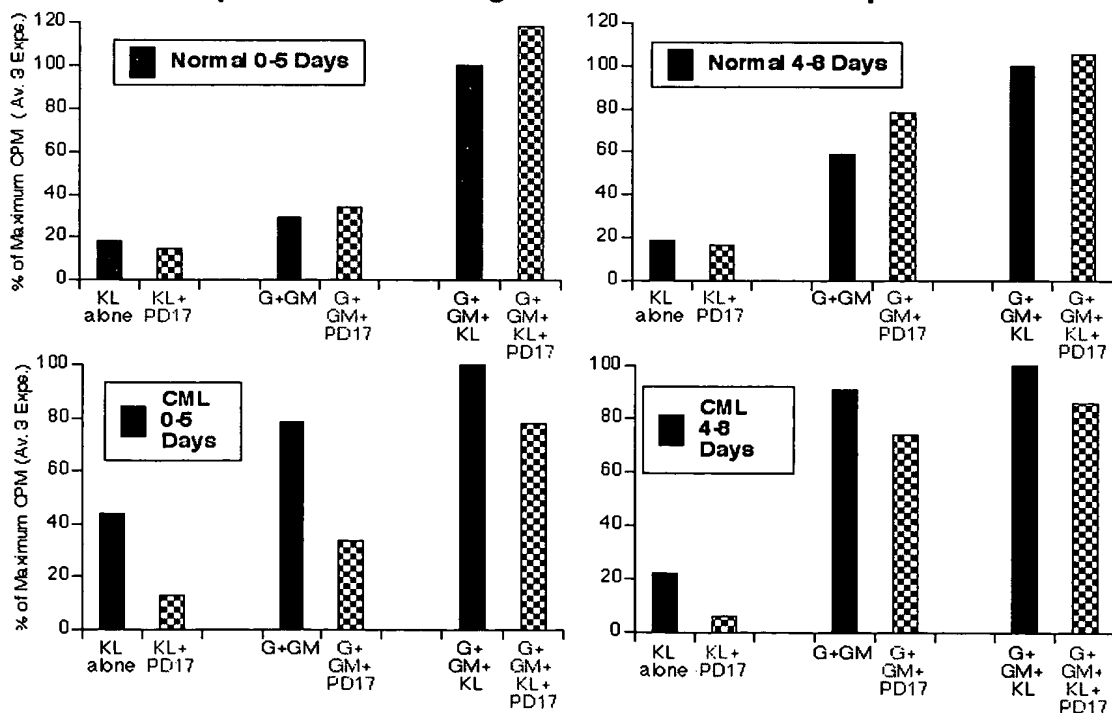
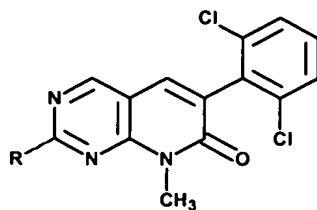


Figure 16

	IC50 (nM)	IC95-99 (nM)
PD166326	0.4	2.5
<b>SKI DV MO-16</b>	0.5	3.5
<b>SKI DV MO-17</b>	0.6	7.5
<b>SKI DV2 43</b>	0.8	7.5
<b>SKI DV1 10</b>	0.8	10
<b>Biotinyl SKI DV1 10</b>	1.5	10
<b>SKI DV2 47</b>	1.5	10
<b>SKI DV 115</b>	2	10
<b>SKI DV2 51</b>	2.5	15
<b>SKI DV2 87</b>	2.5	20
<b>SKI DV2 37</b>	7.5	50
<b>SKI DV2 53</b>	15	100
<b>SKI DV2 71</b>	20	200
<b>SKI DV2 35</b>	350	10000
<b>SKI DV2 33</b>	4000	>10000
<b>SKI DV 103</b>	10000	>10000

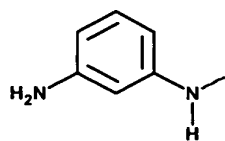
**Figure 17**

**A**

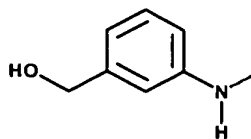


6-(2,6-dichlorophenyl)-8-methylpyrido[2,3-d]pyrimidin-7(8H)-one

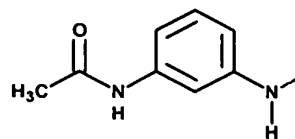
**B**



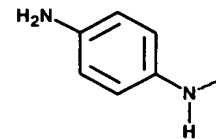
SKI DV 2-43



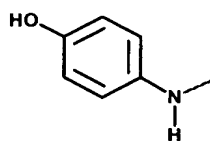
PD166326



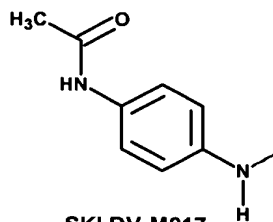
SKI DV-M016



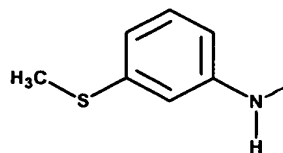
SKI DV 1-10



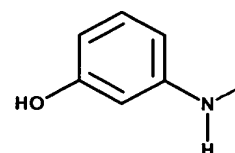
SKI DV 2-47



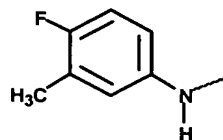
SKI DV-M017



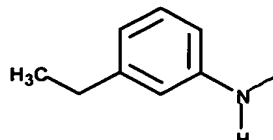
PD173955



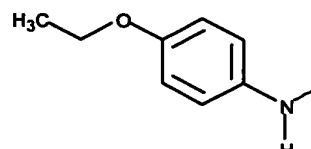
SKI DV 2-89



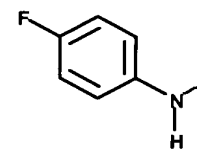
PD180970



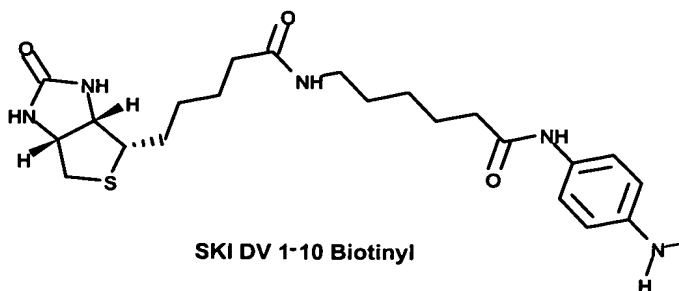
SKI DV 2 87



PD173958



PD173956

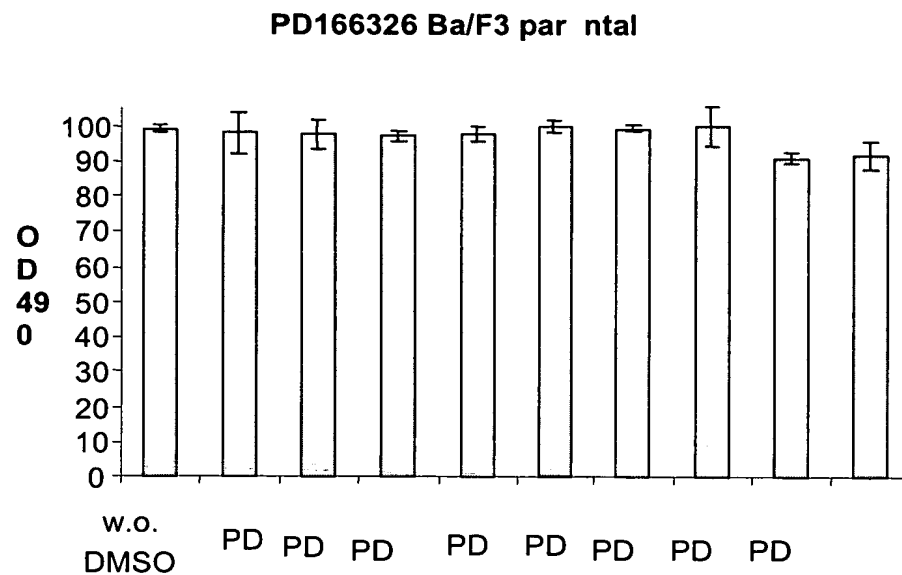


SKI DV 1-10 Biotinyl

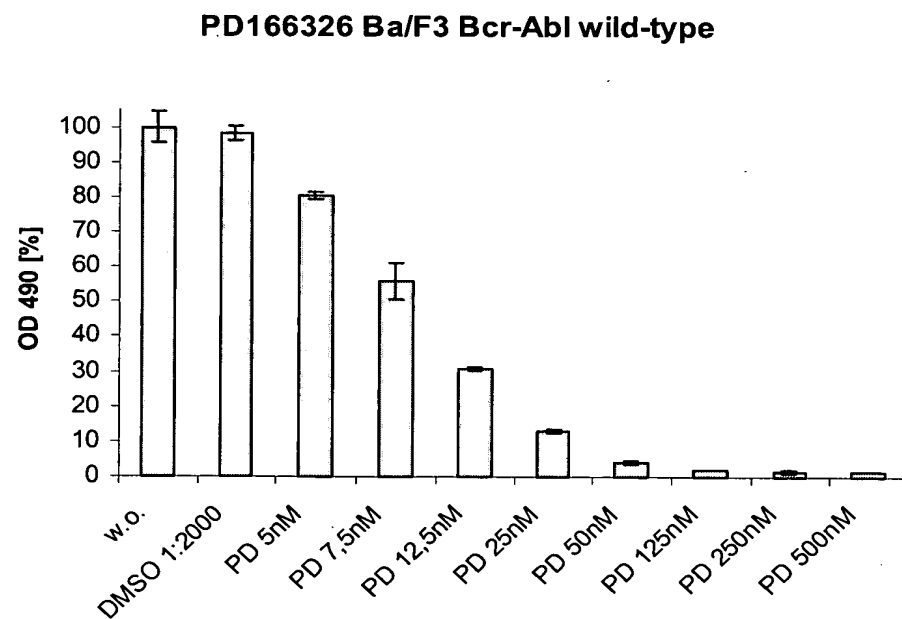
**Figure 18**



**A**

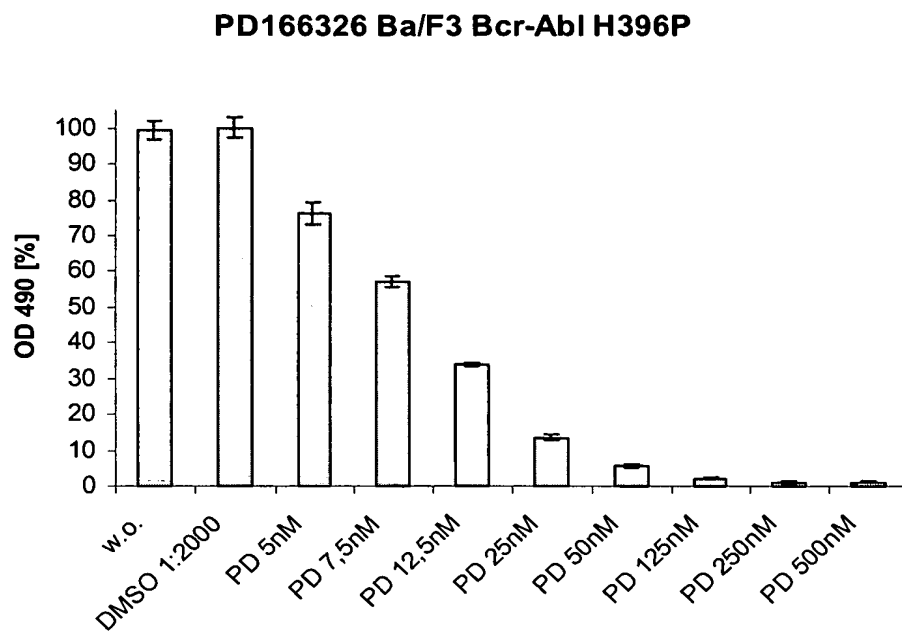


**B**

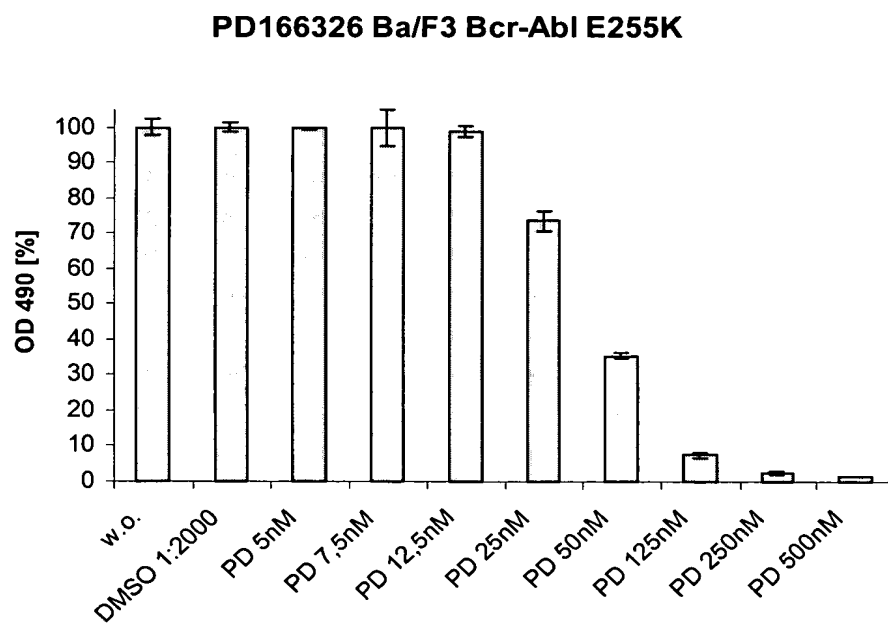


**Figure 19A**

**C**

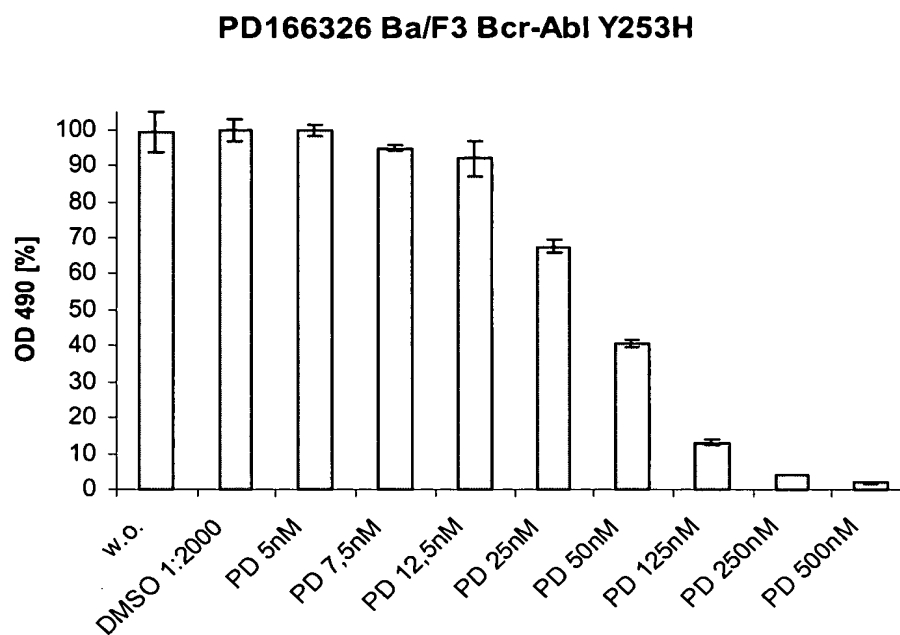


**D**

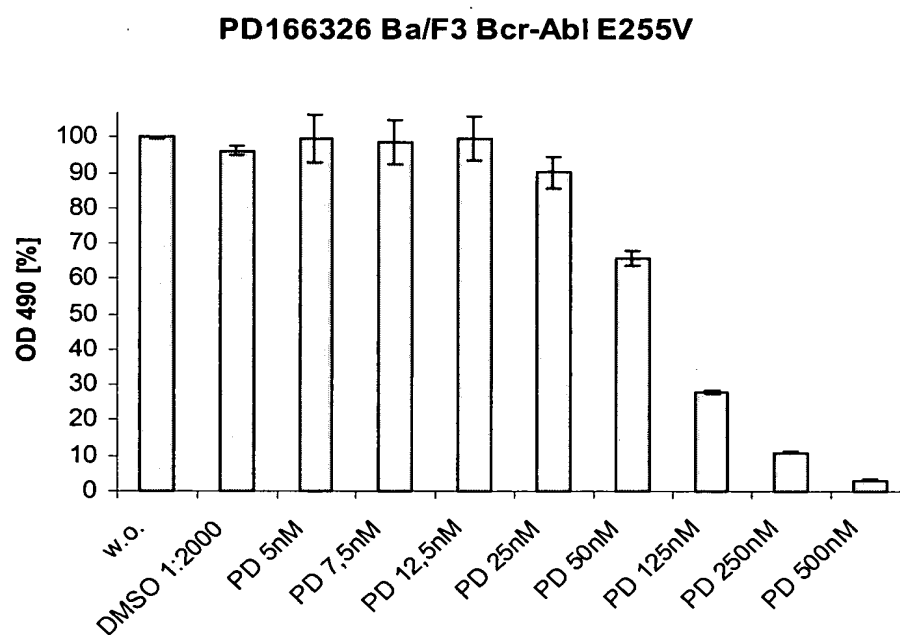


**Figure 19B**

**E**

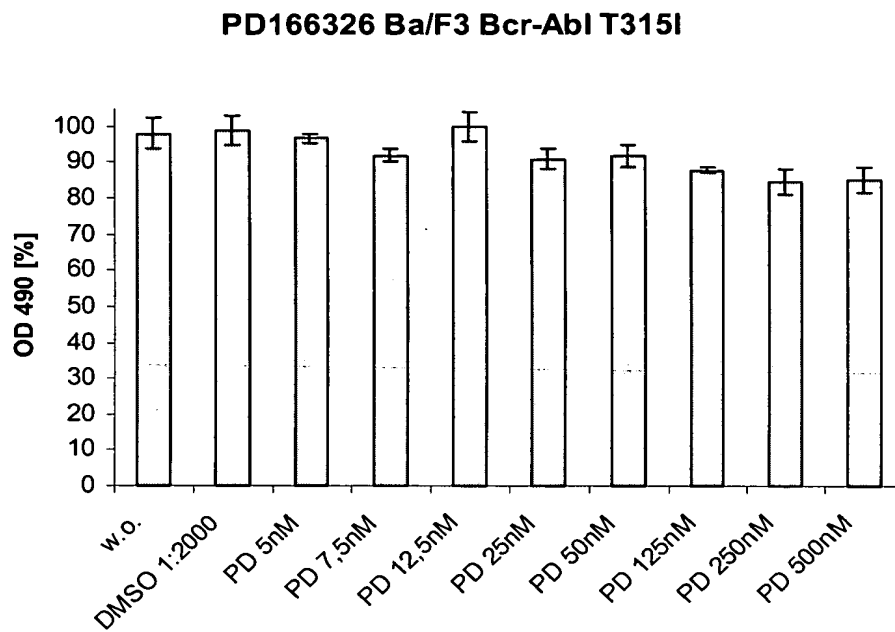


**F**



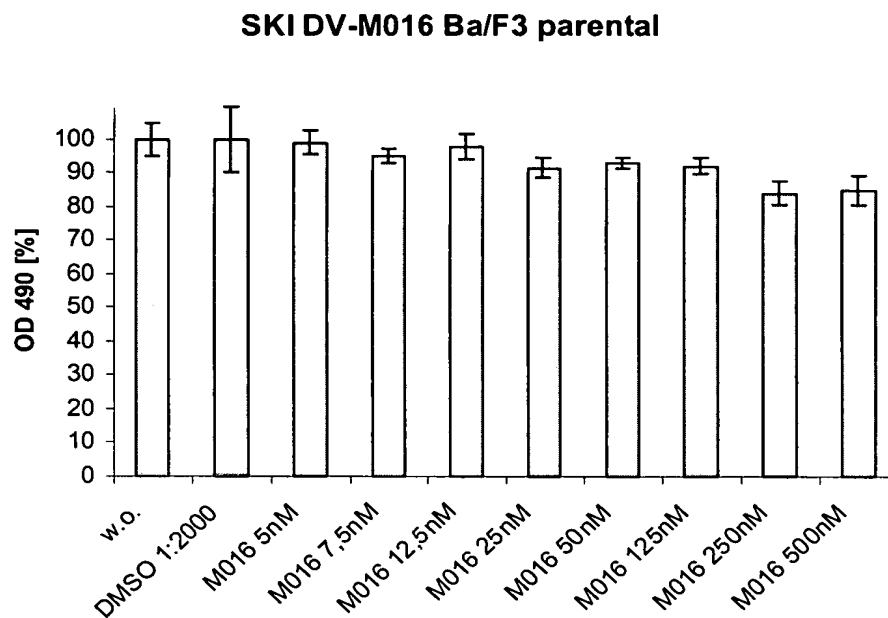
**Figure 19C**

**G**

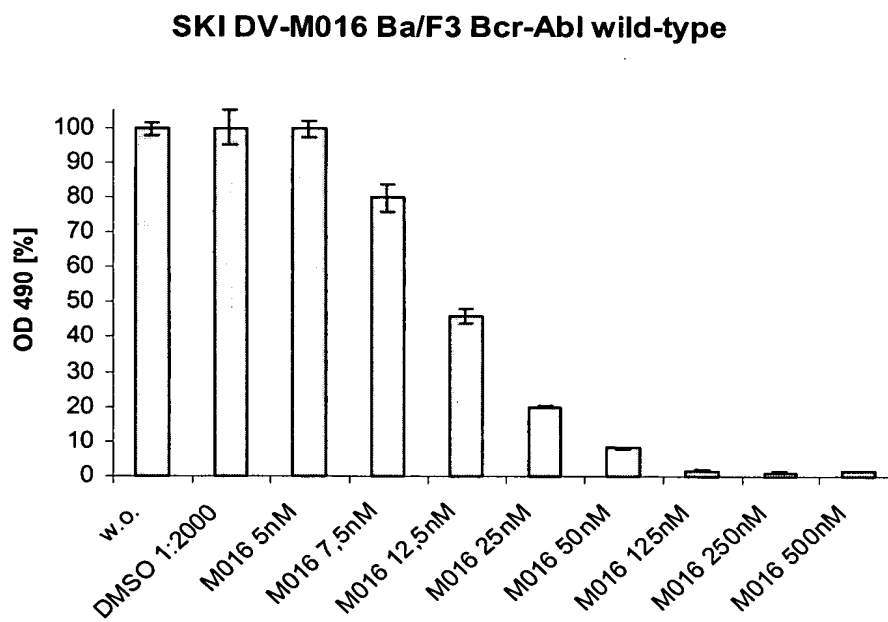


**Figure 19D**

**A**

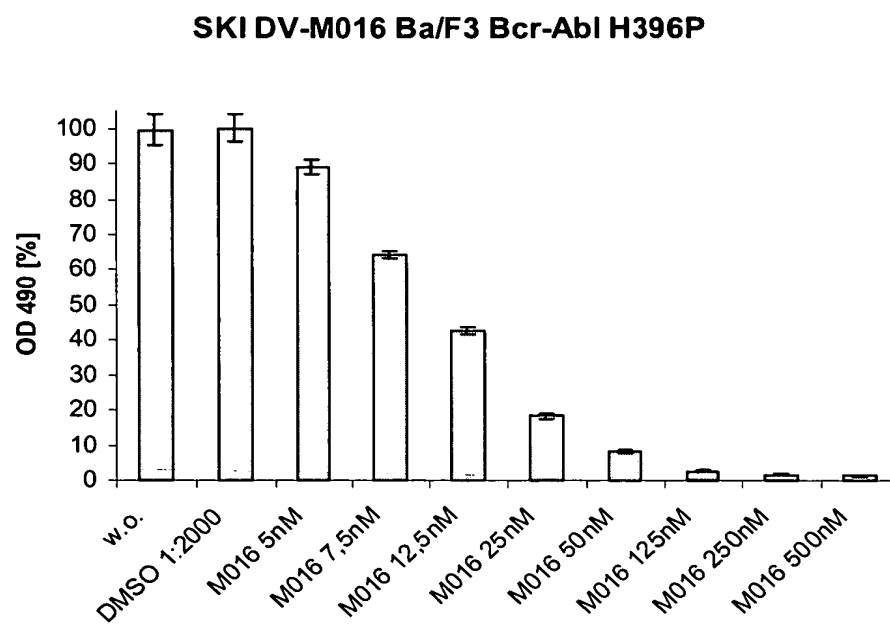


**B**

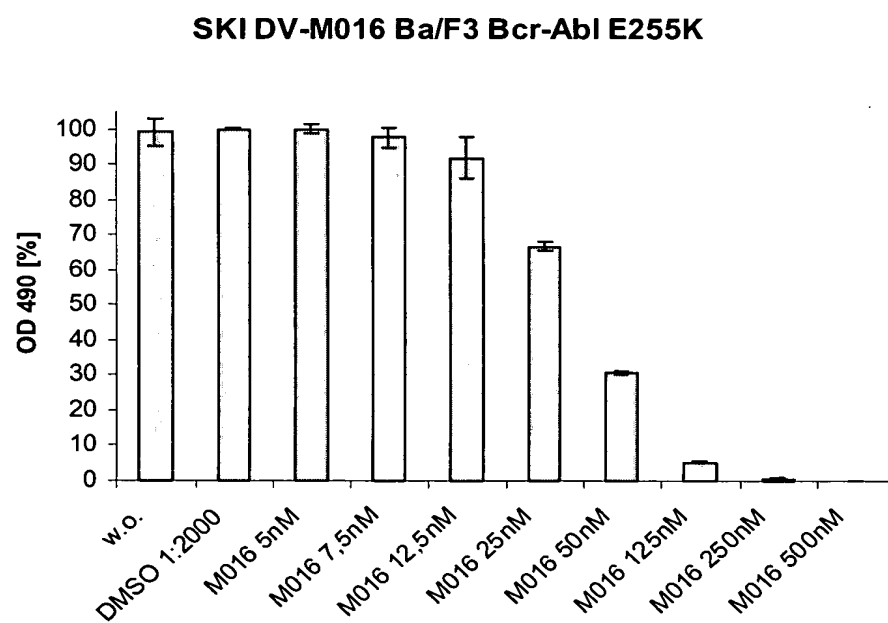


**Figure 20A**

**C**

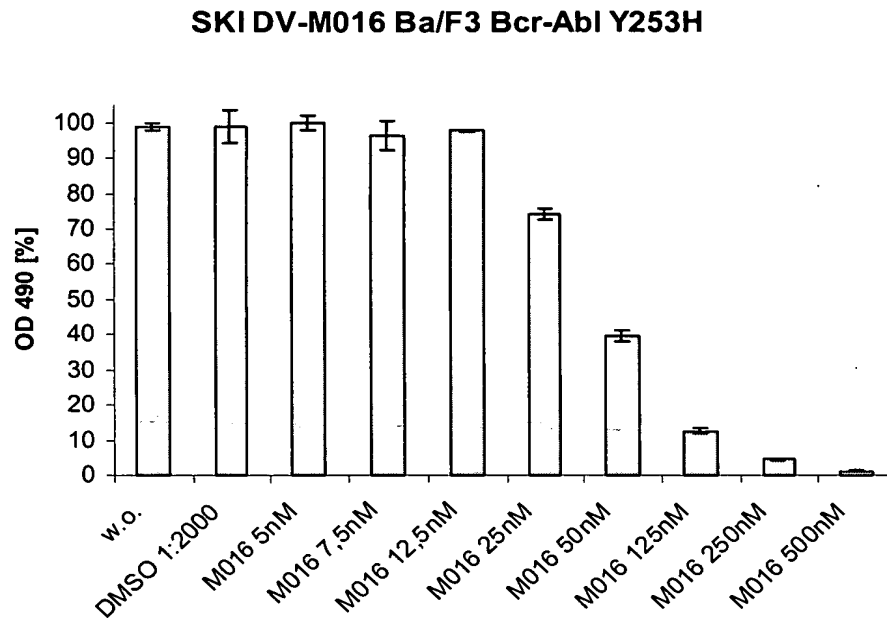


**D**

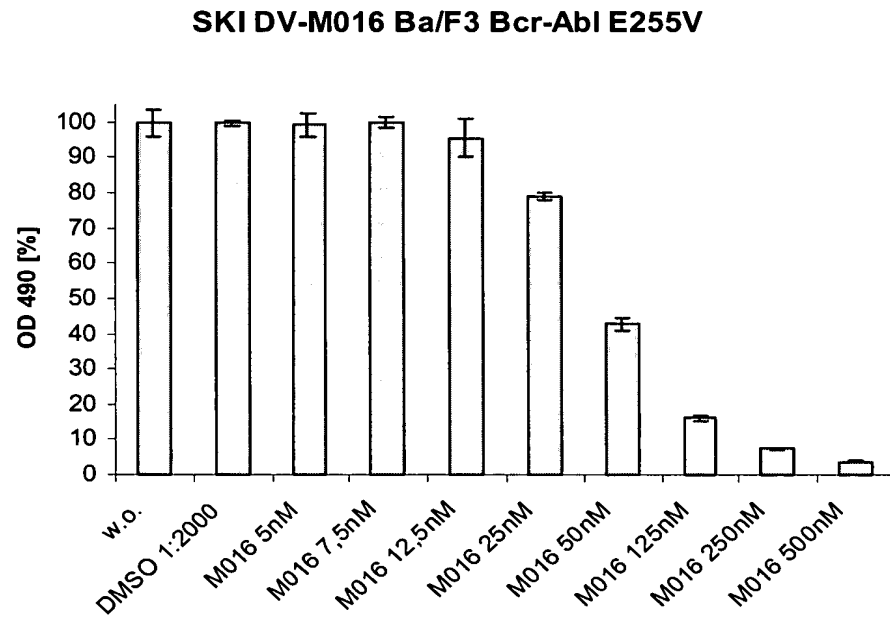


**Figure 20B**

**E**

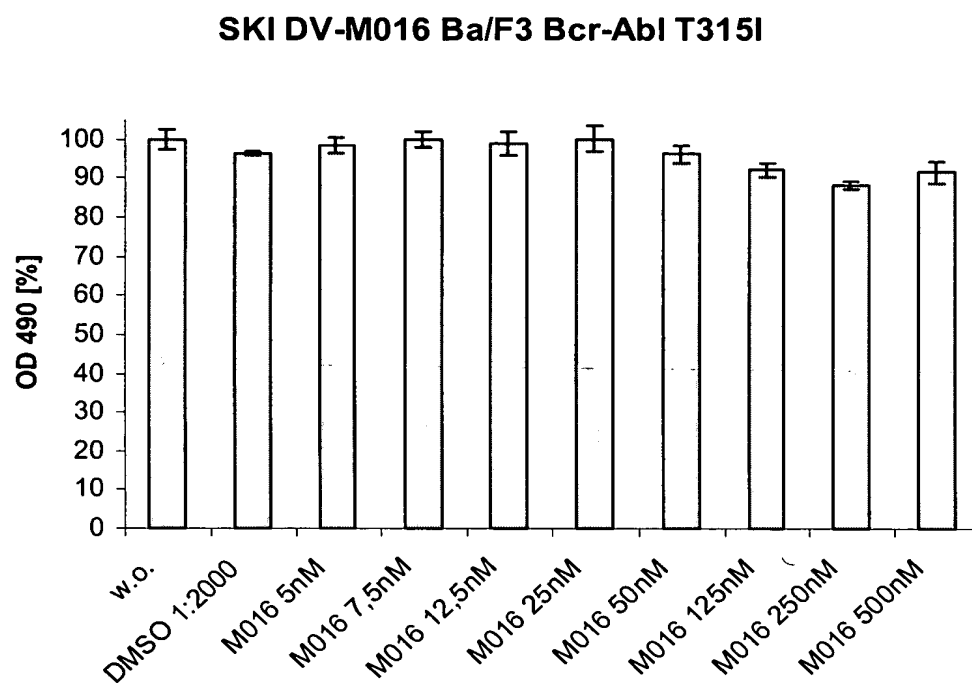


**F**



**Figure 20C**

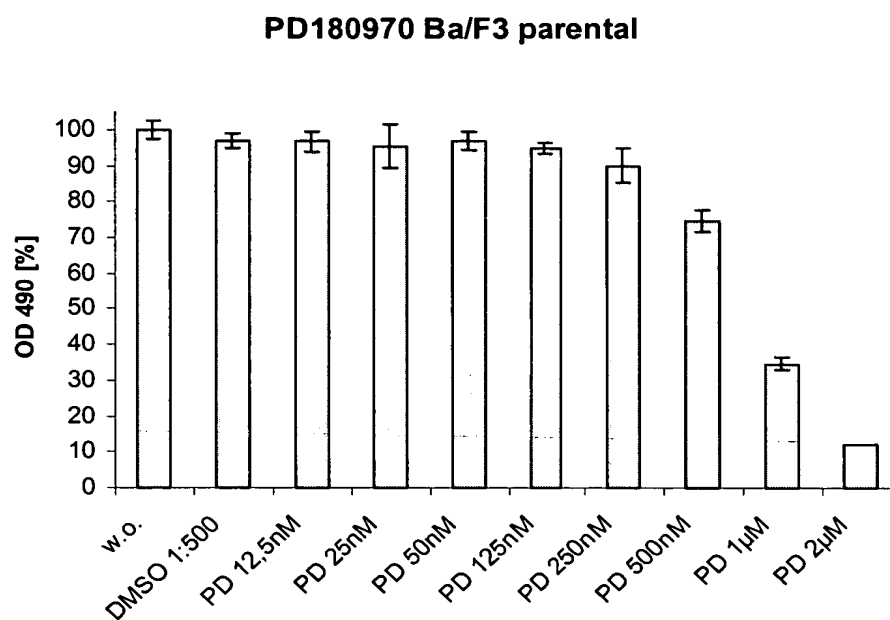
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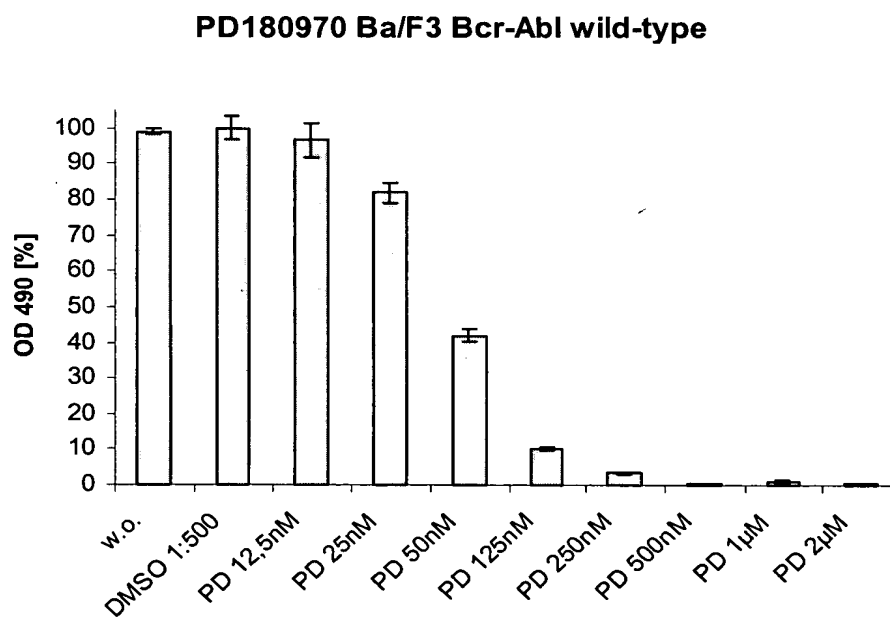
**Figure 20D**



**A**

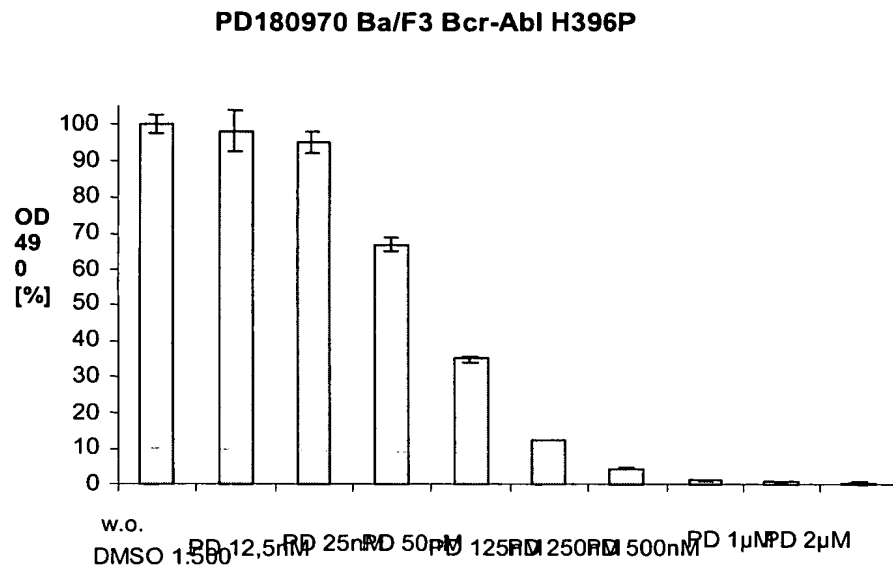


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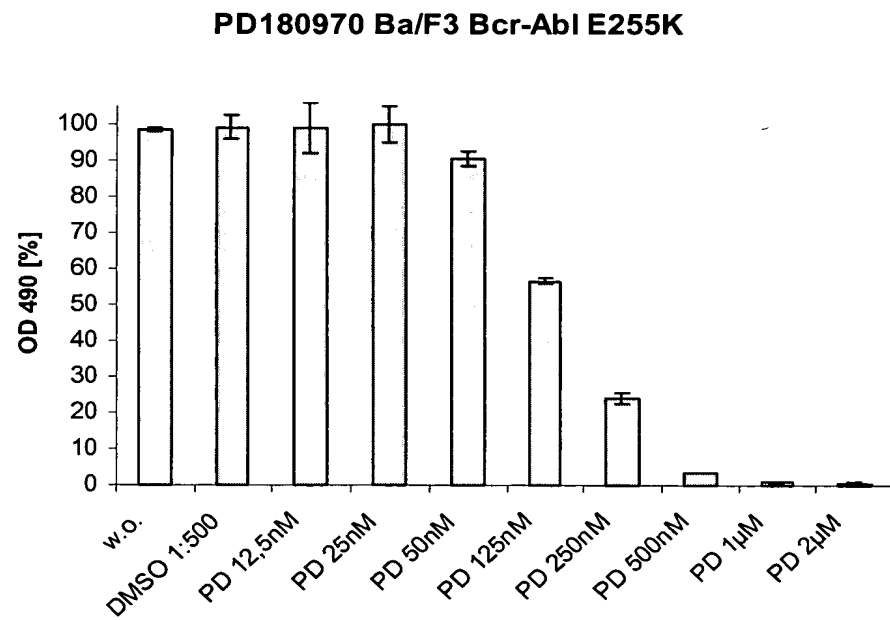


**Figure 21A**

**C**

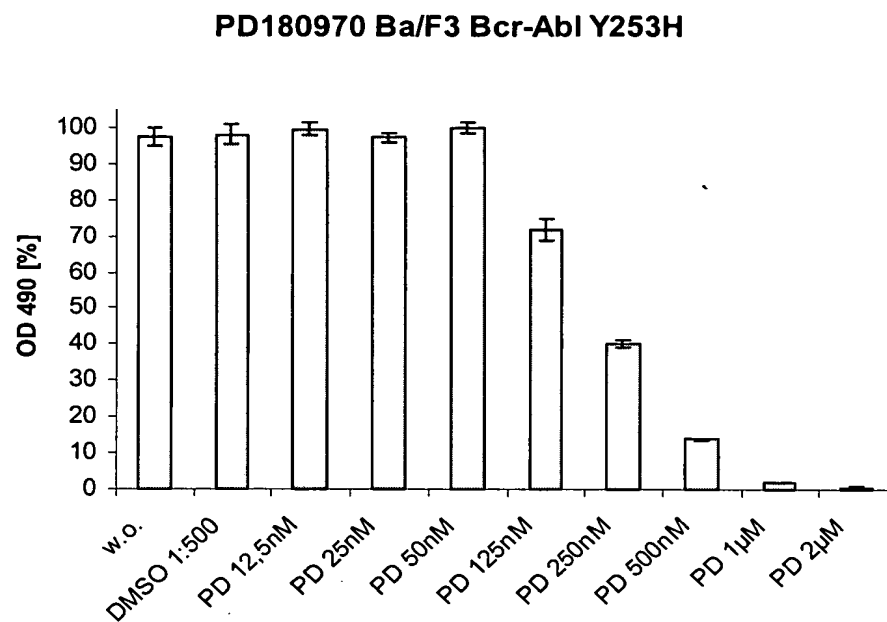


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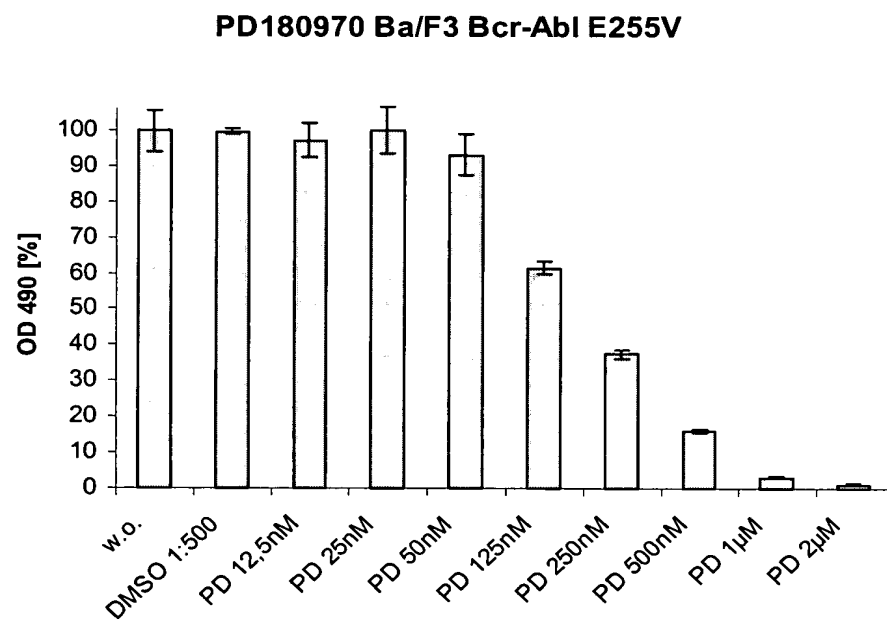


**Figure 21B**

**E**

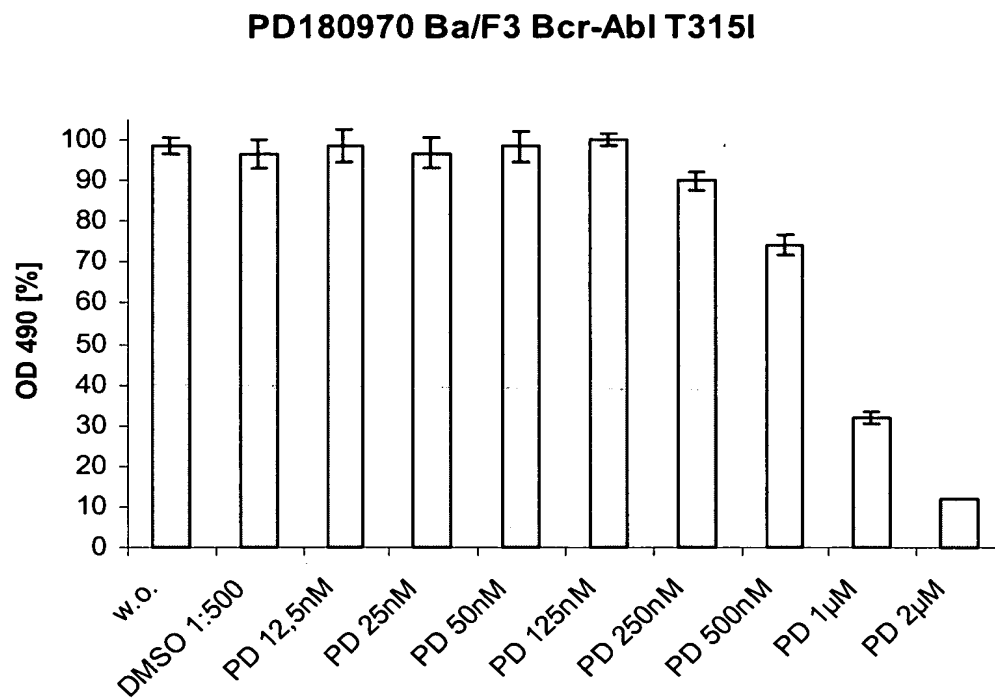


**F**

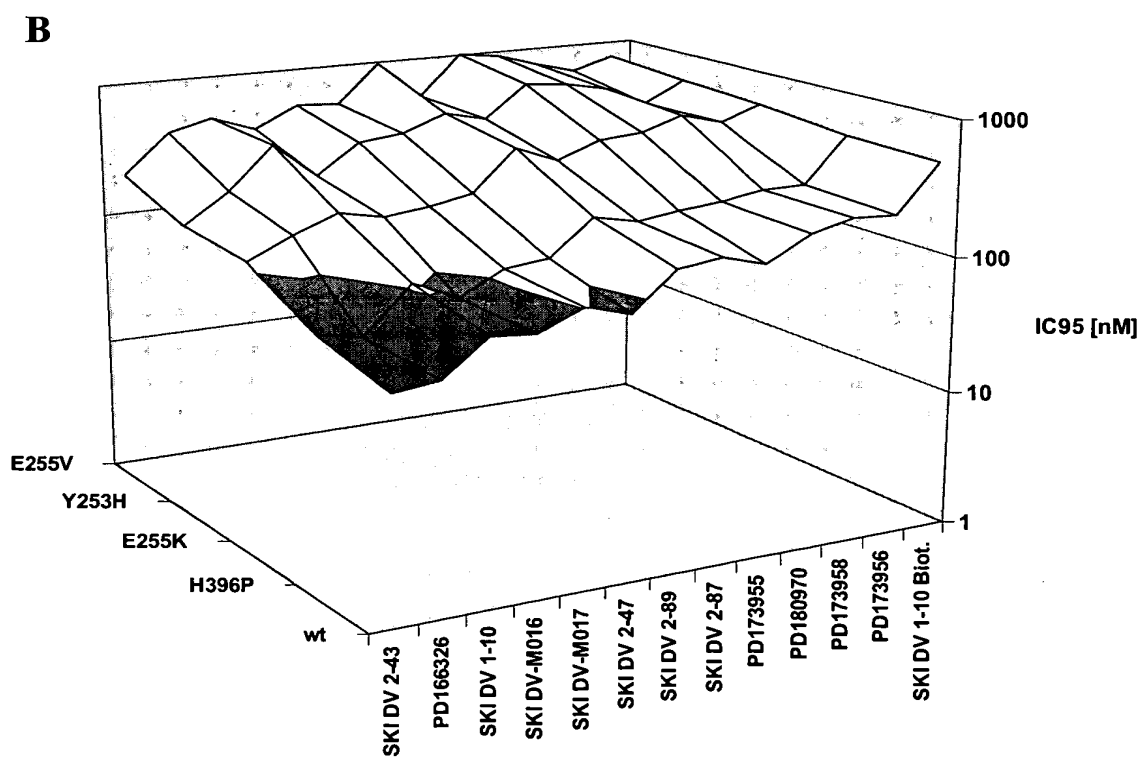
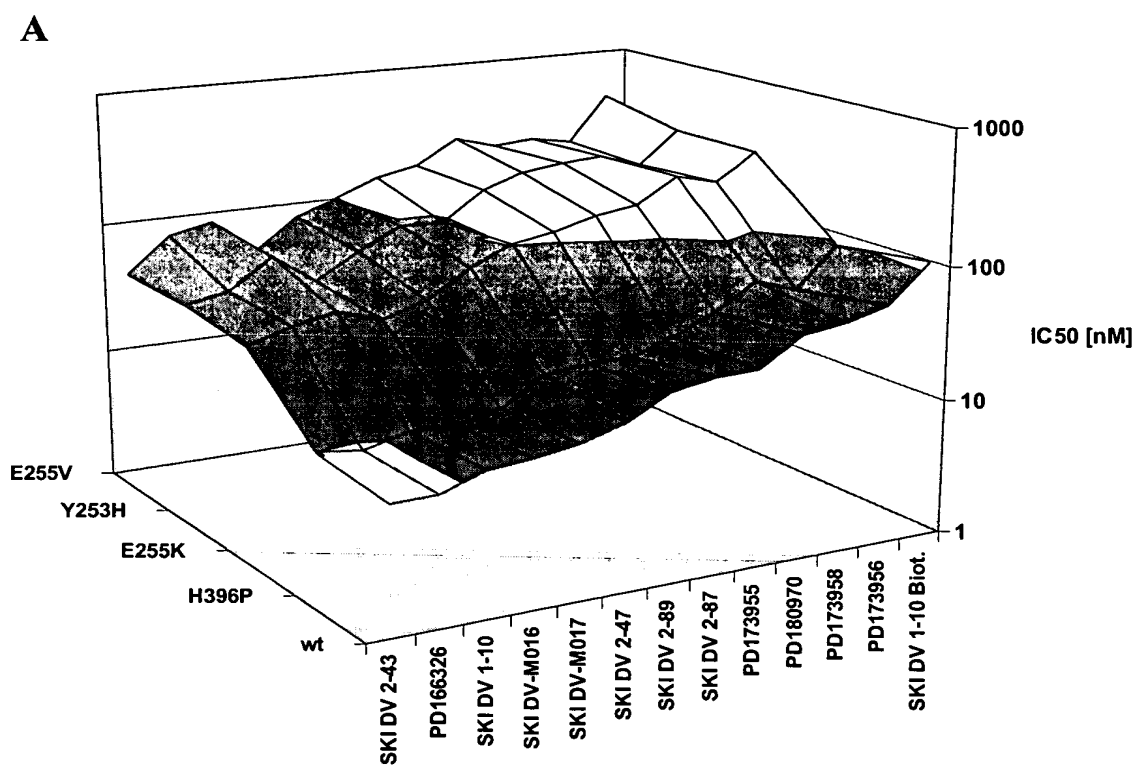


**Figure 21C**

**G**



**Figure 21D**



**Figure 22**

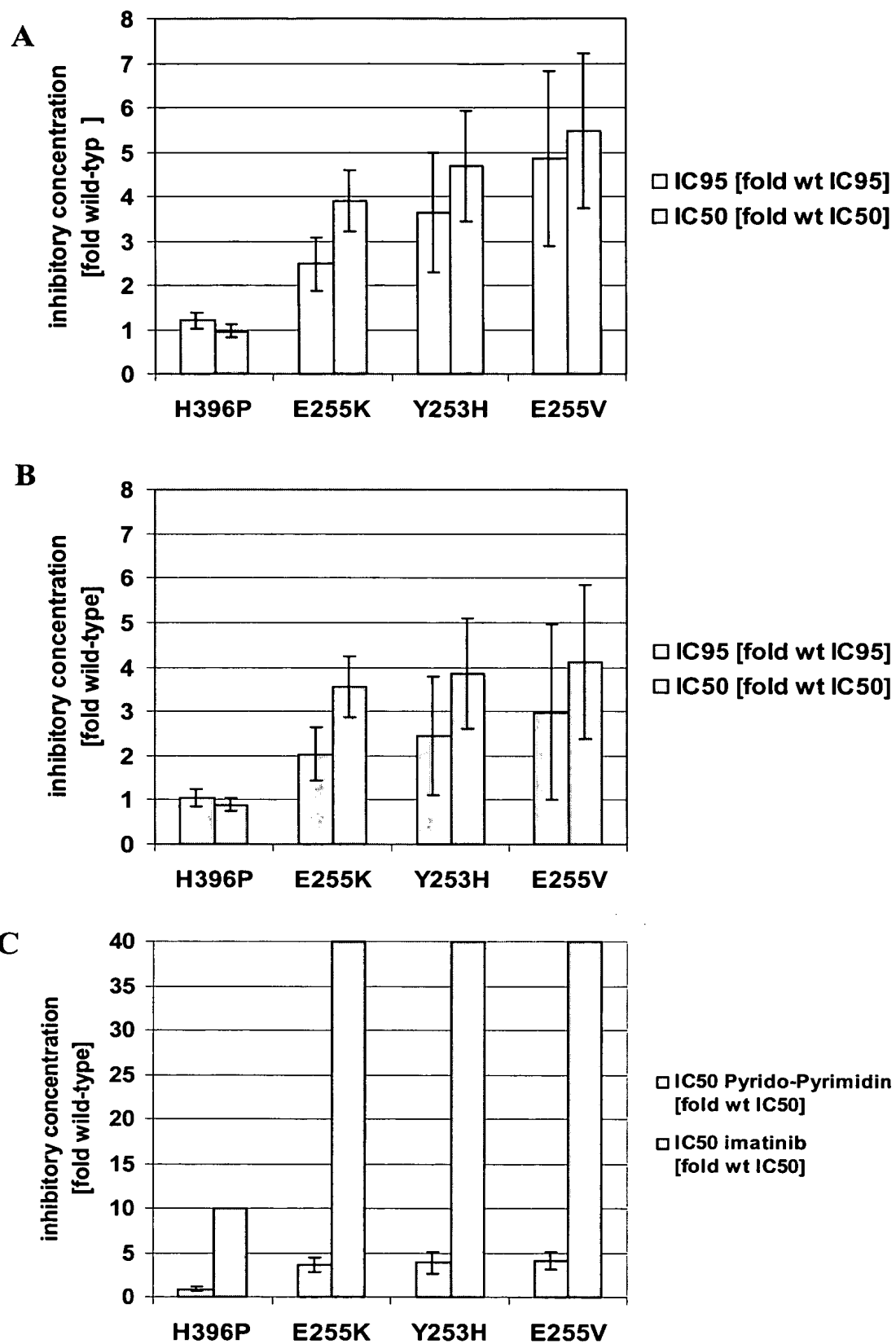


Figure 23

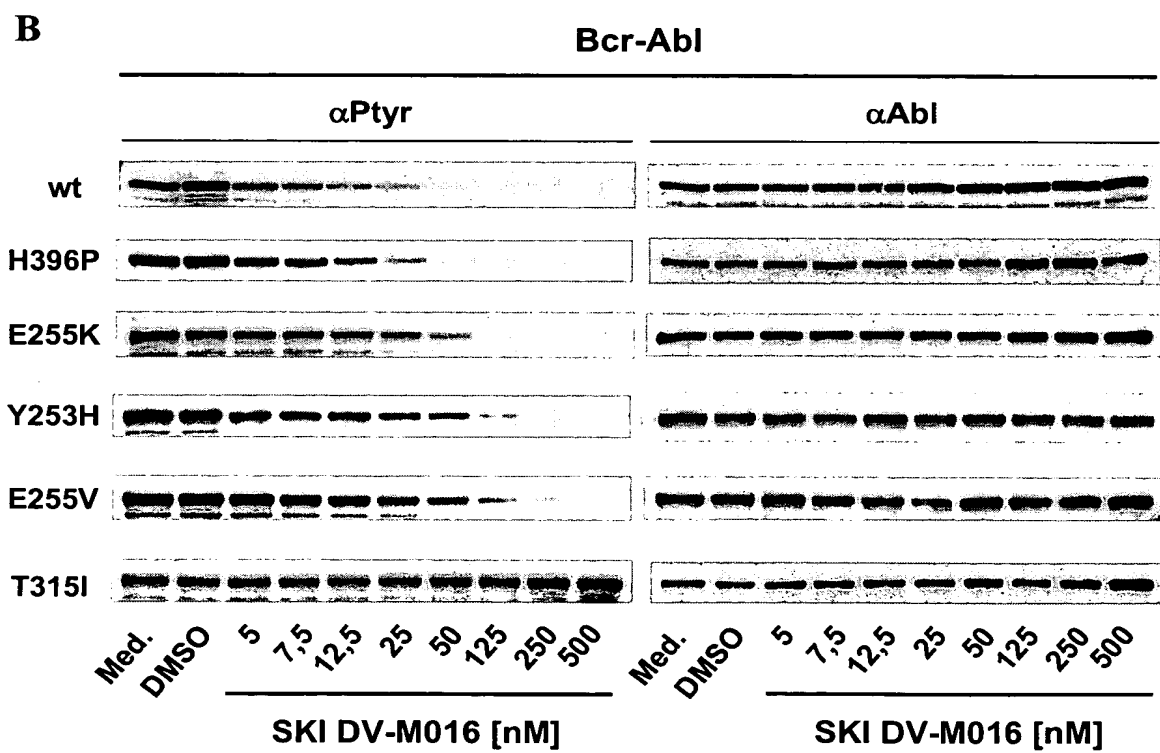
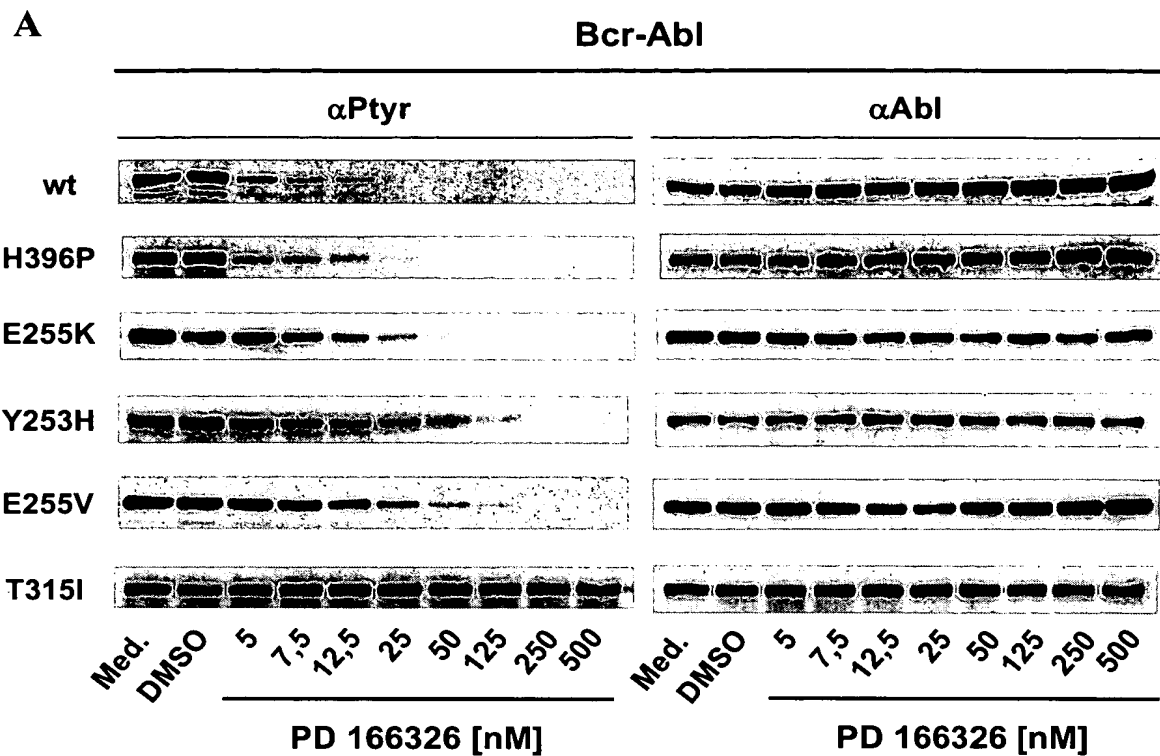


Figure 24

C

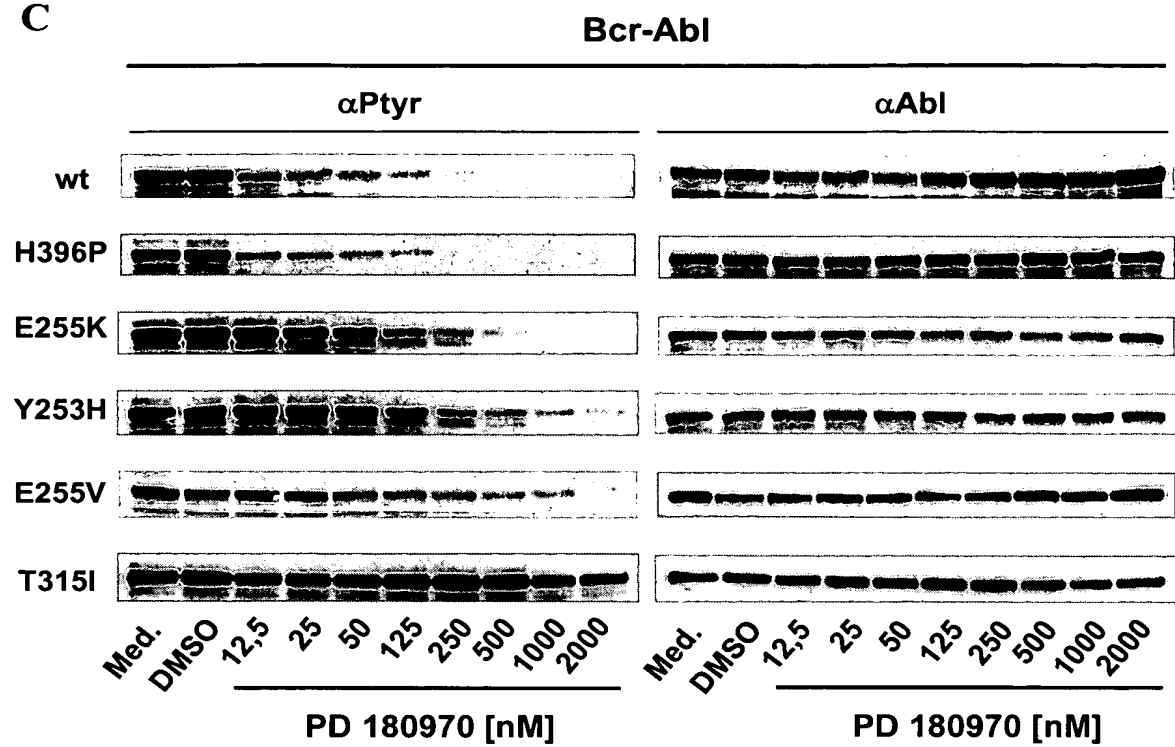
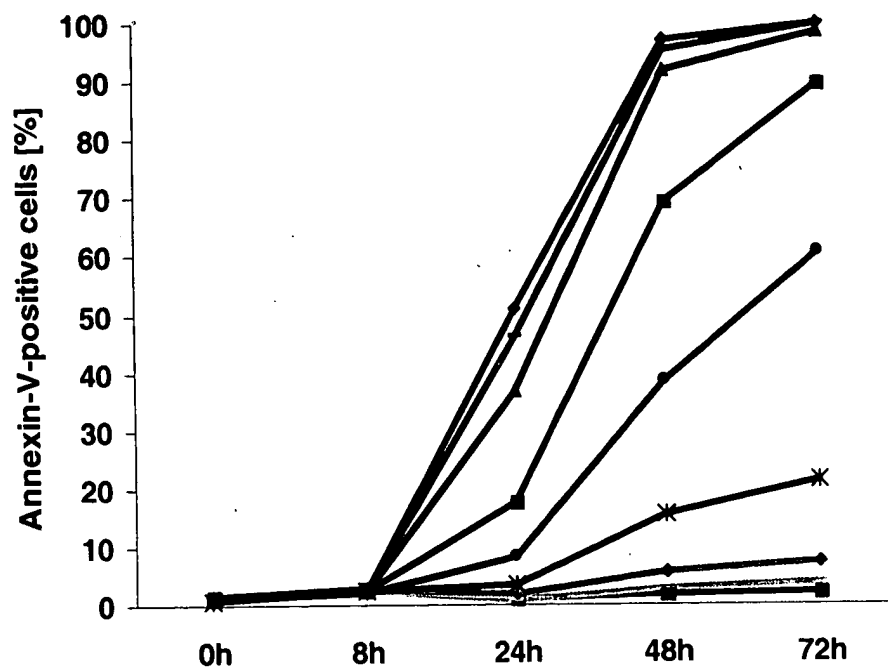


Figure 24B



A



B

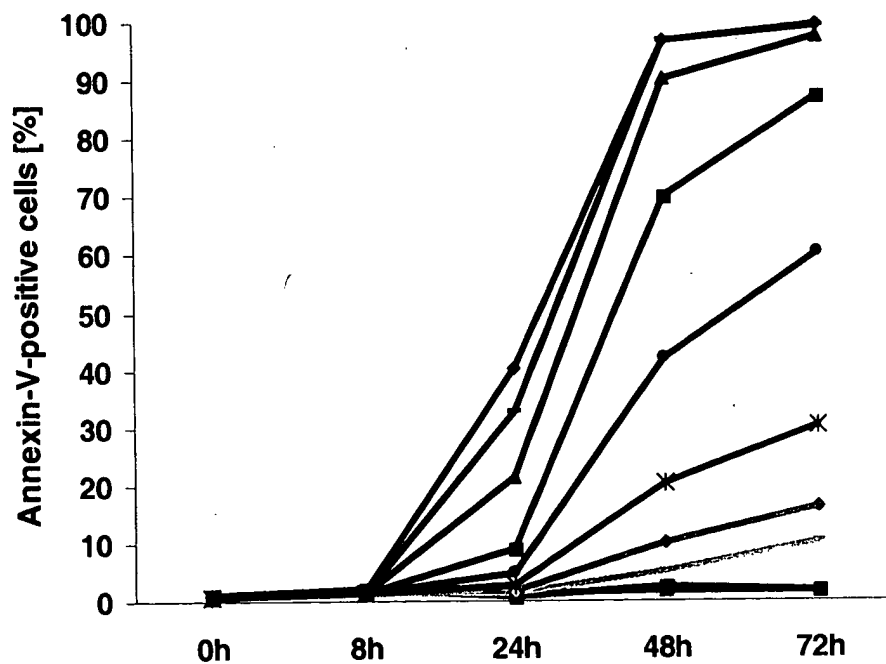
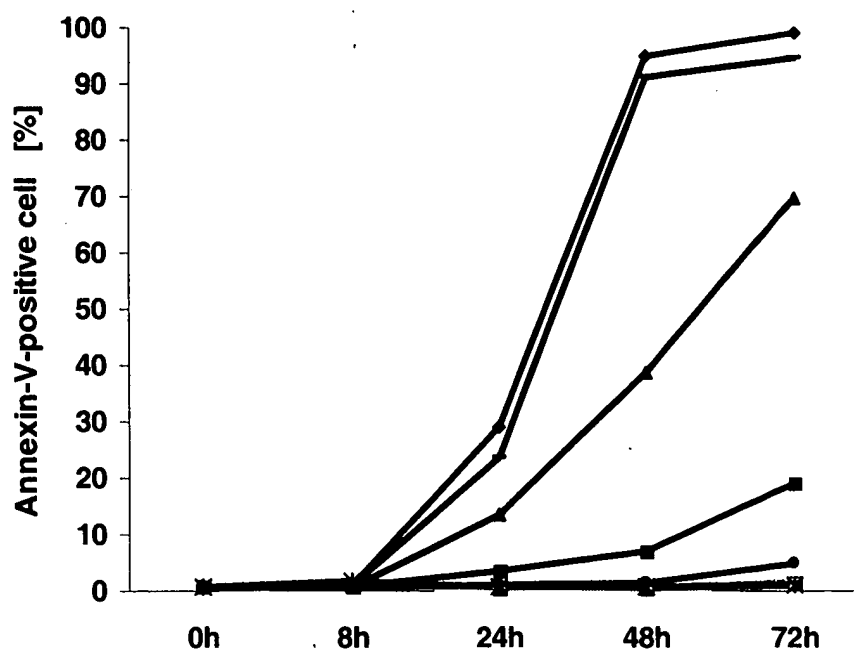


Figure 25A

- Medium
- DMSO
- PD166326 5nM
- PD166326 7,5nM
- PD166326 12,5nM
- PD166326 25nM
- PD166326 50nM
- PD166326 125nM
- PD166326 250nM
- PD166326 500nM

C



D

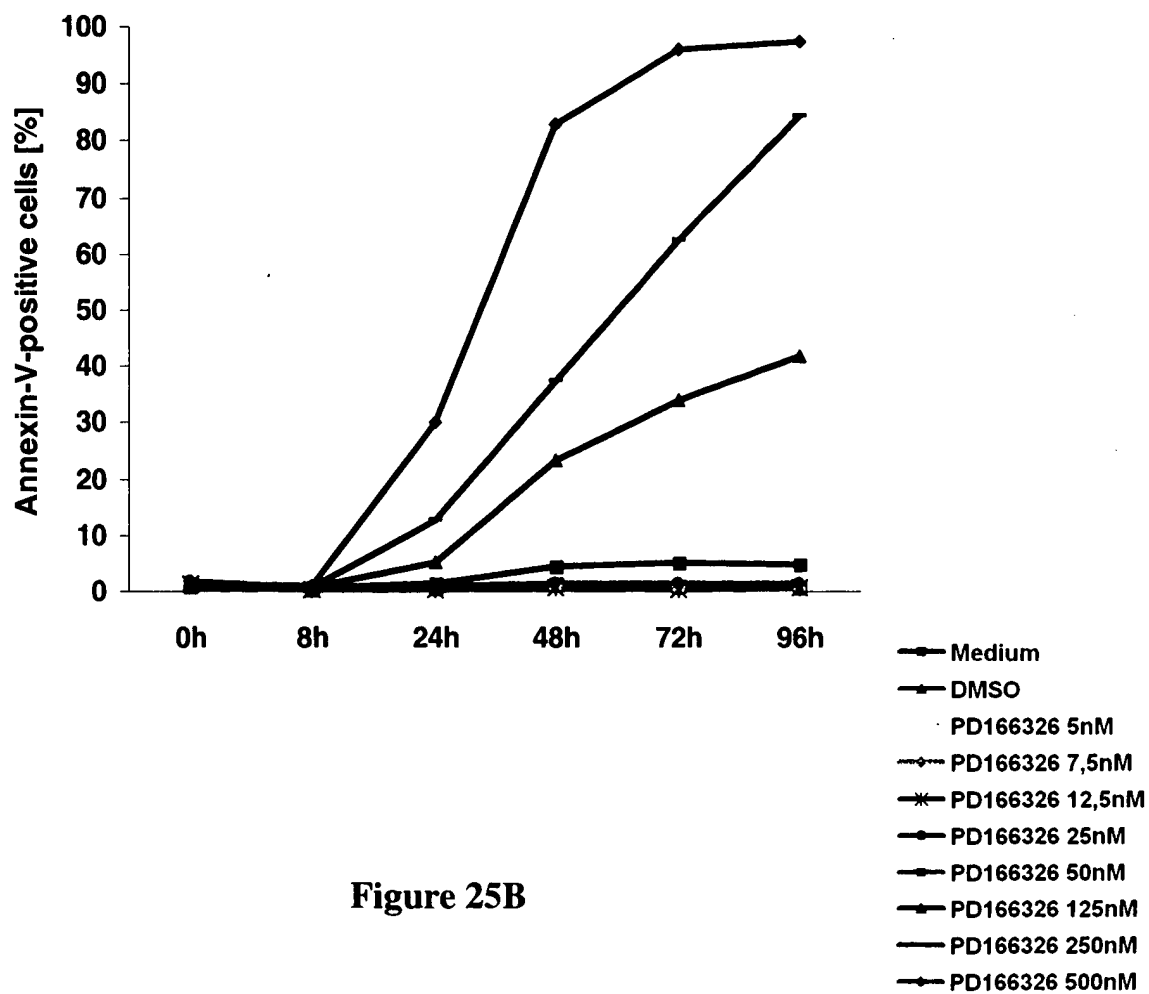
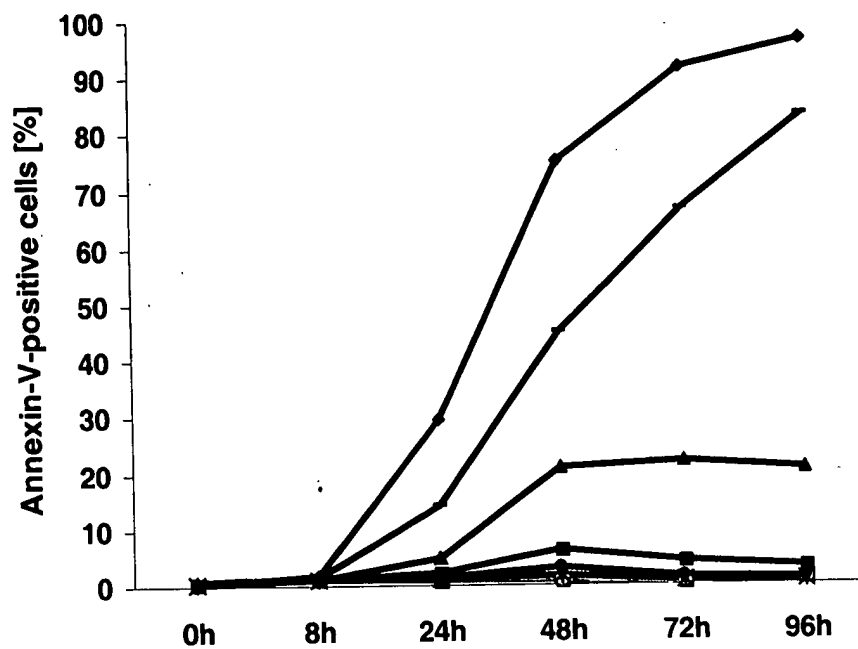


Figure 25B

E



F

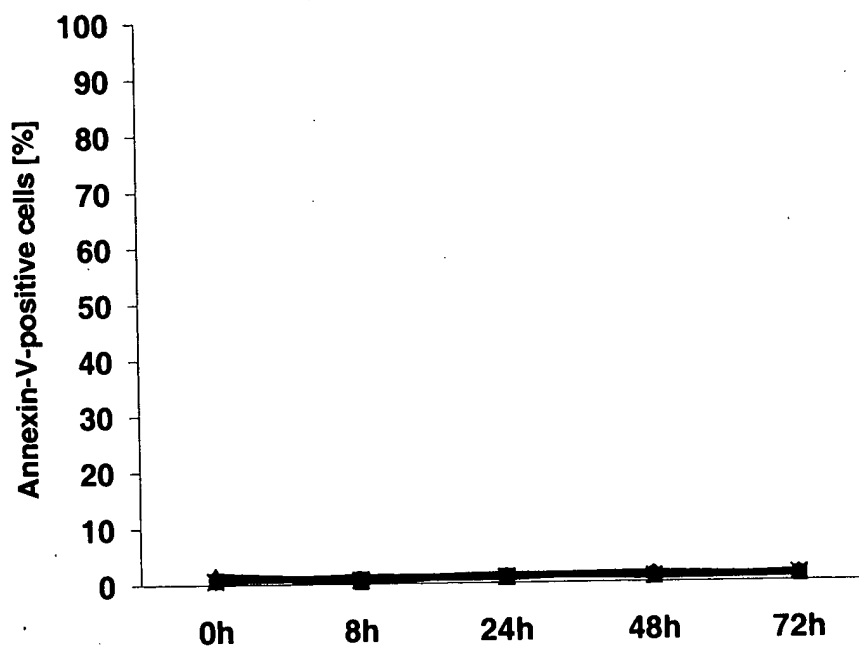


Figure 25C

- Medium
- DMSO
- PD166326 5nM
- PD166326 7,5nM
- PD166326 12,5nM
- PD166326 25nM
- PD166326 50nM
- PD166326 125nM
- PD166326 250nM
- PD166326 500nM

G

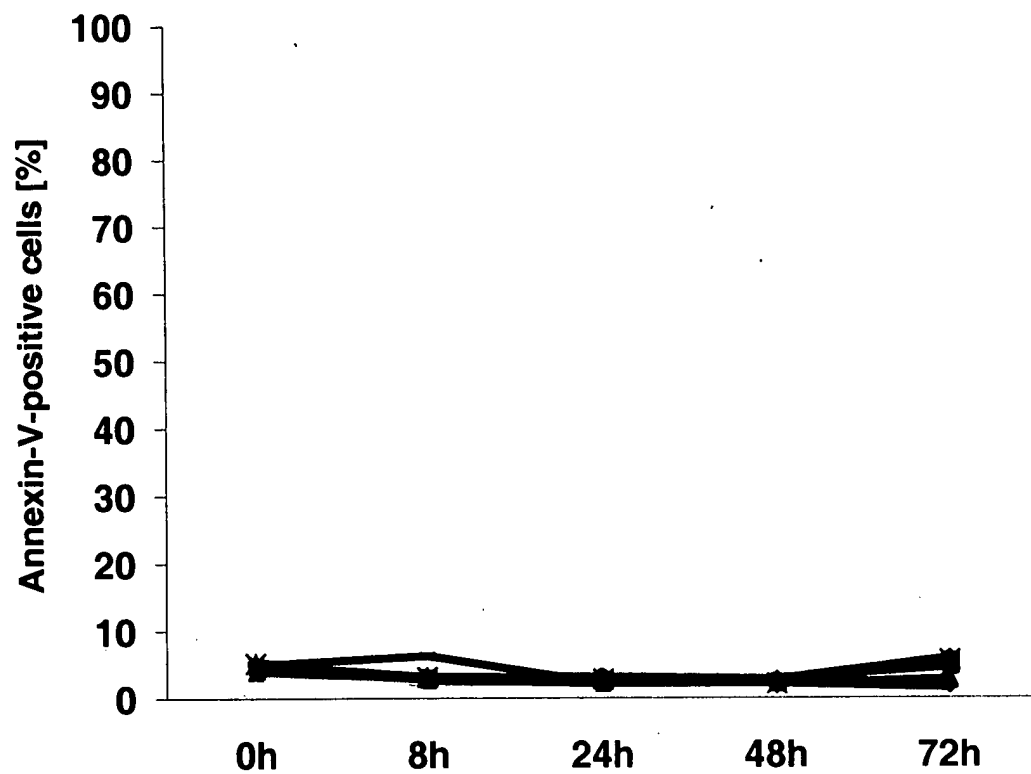
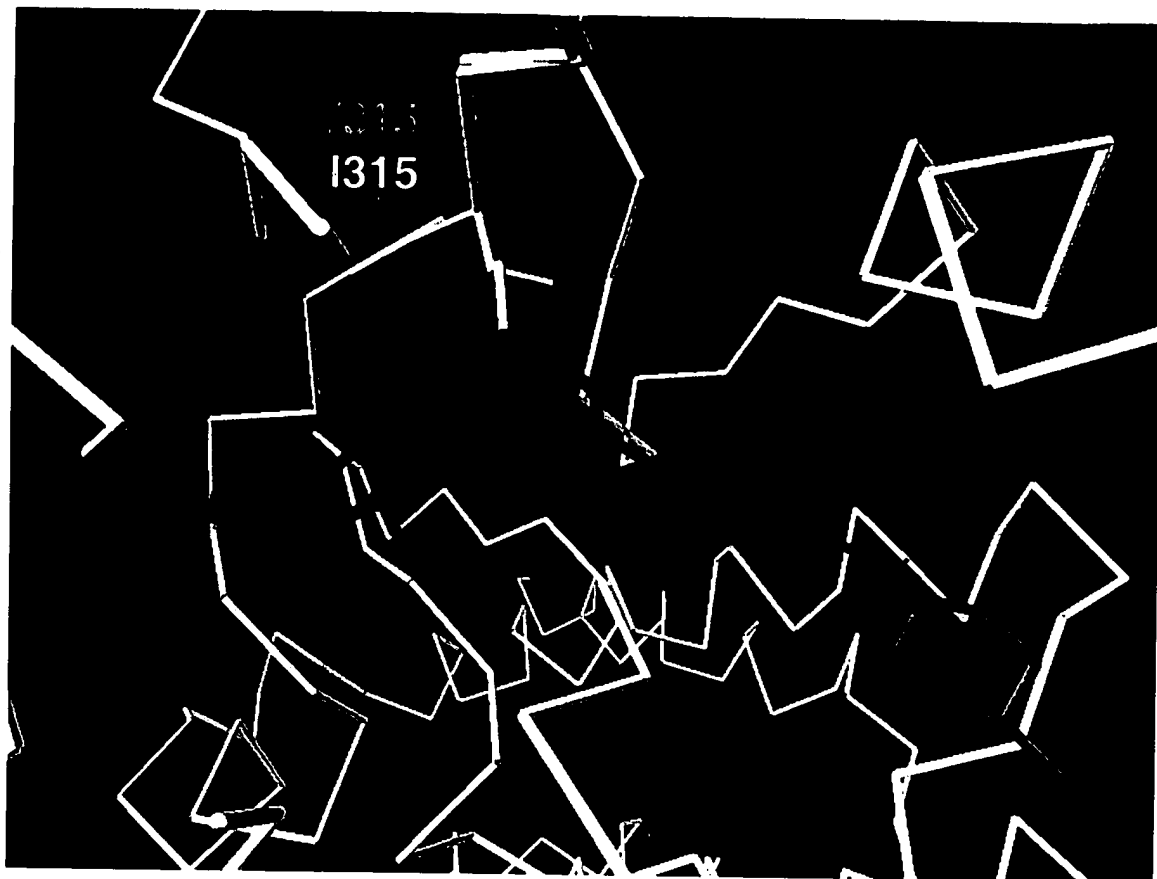
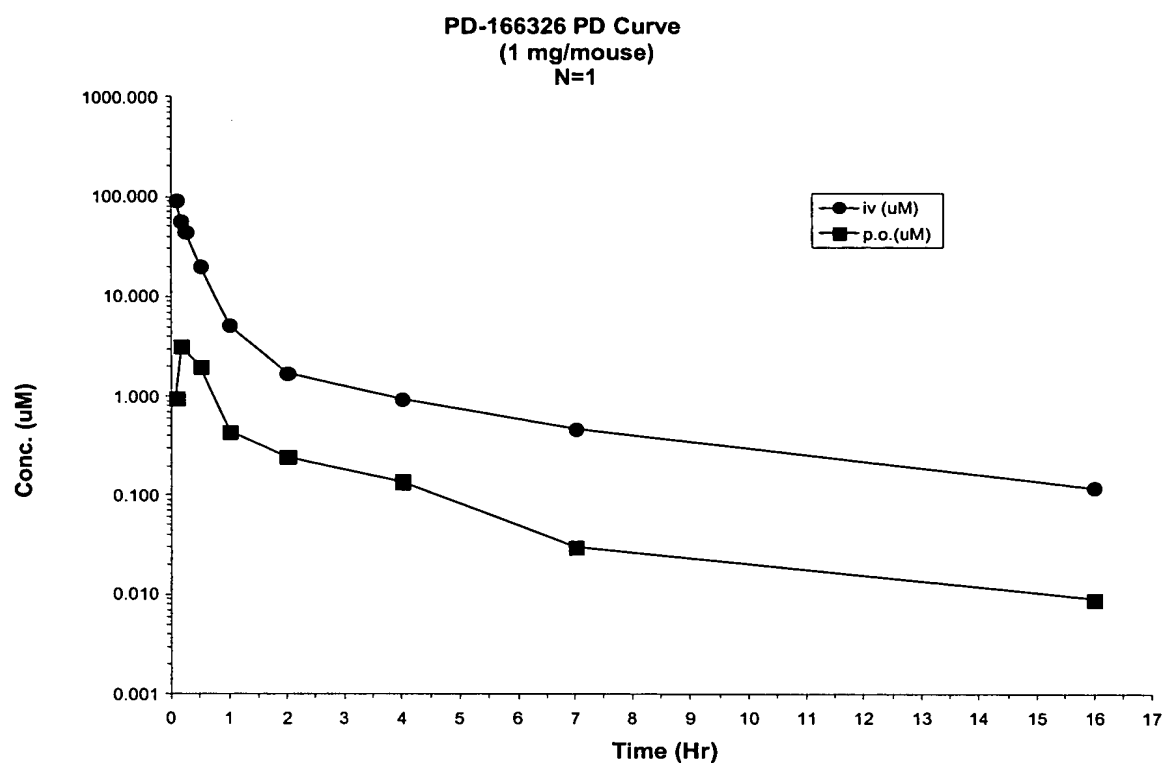


Figure 25D

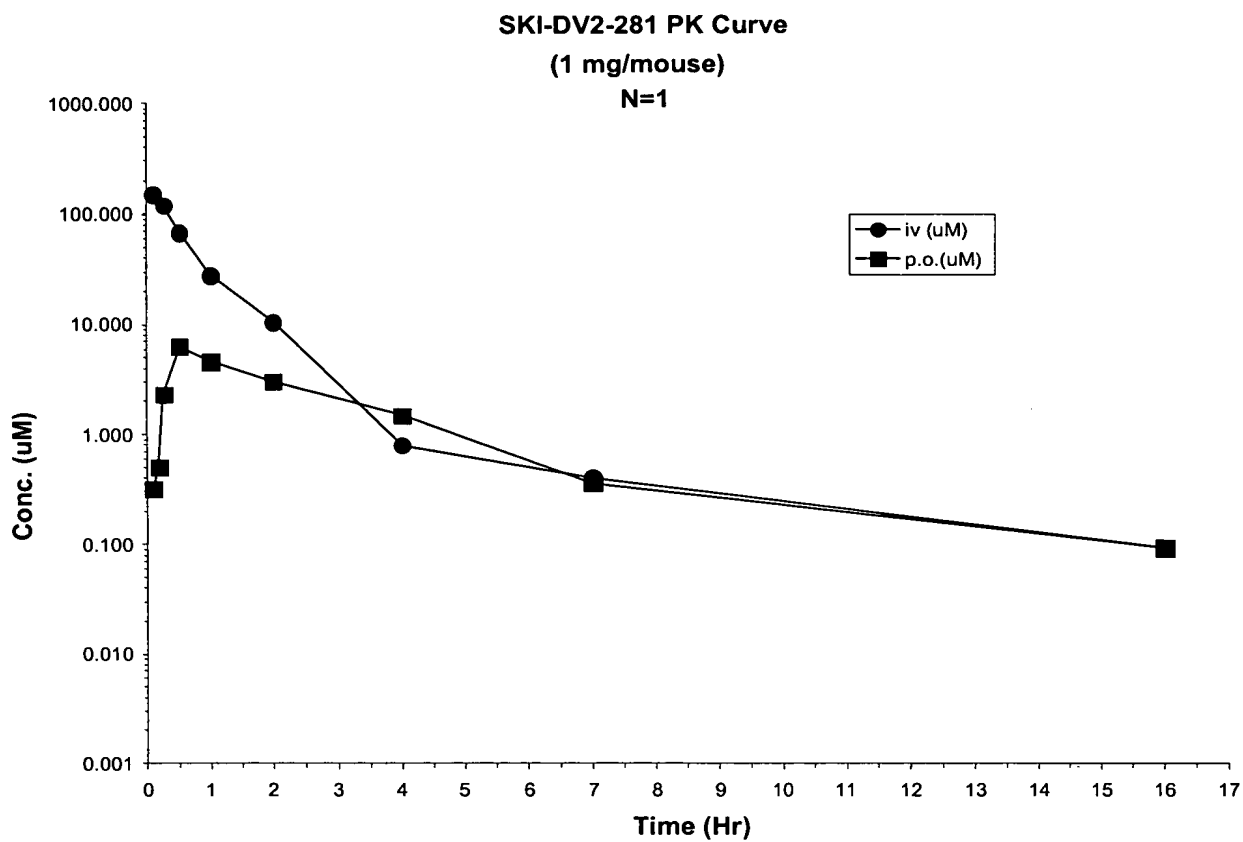
- Medium
- DMSO
- PD166326 5nM
- PD166326 7,5nM
- \*— PD166326 12,5nM
- PD166326 25nM
- PD166326 50nM
- PD166326 125nM
- PD166326 250nM
- PD166326 500nM



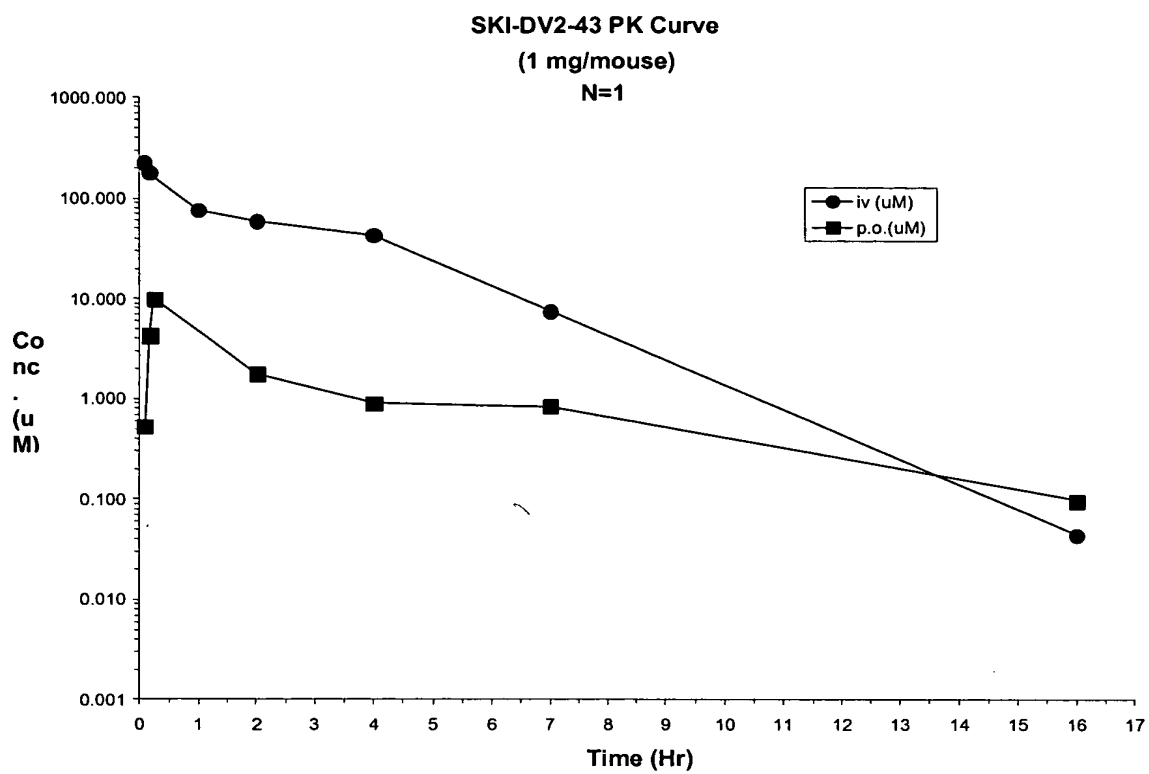
**Figure 26**



**Figure 27**



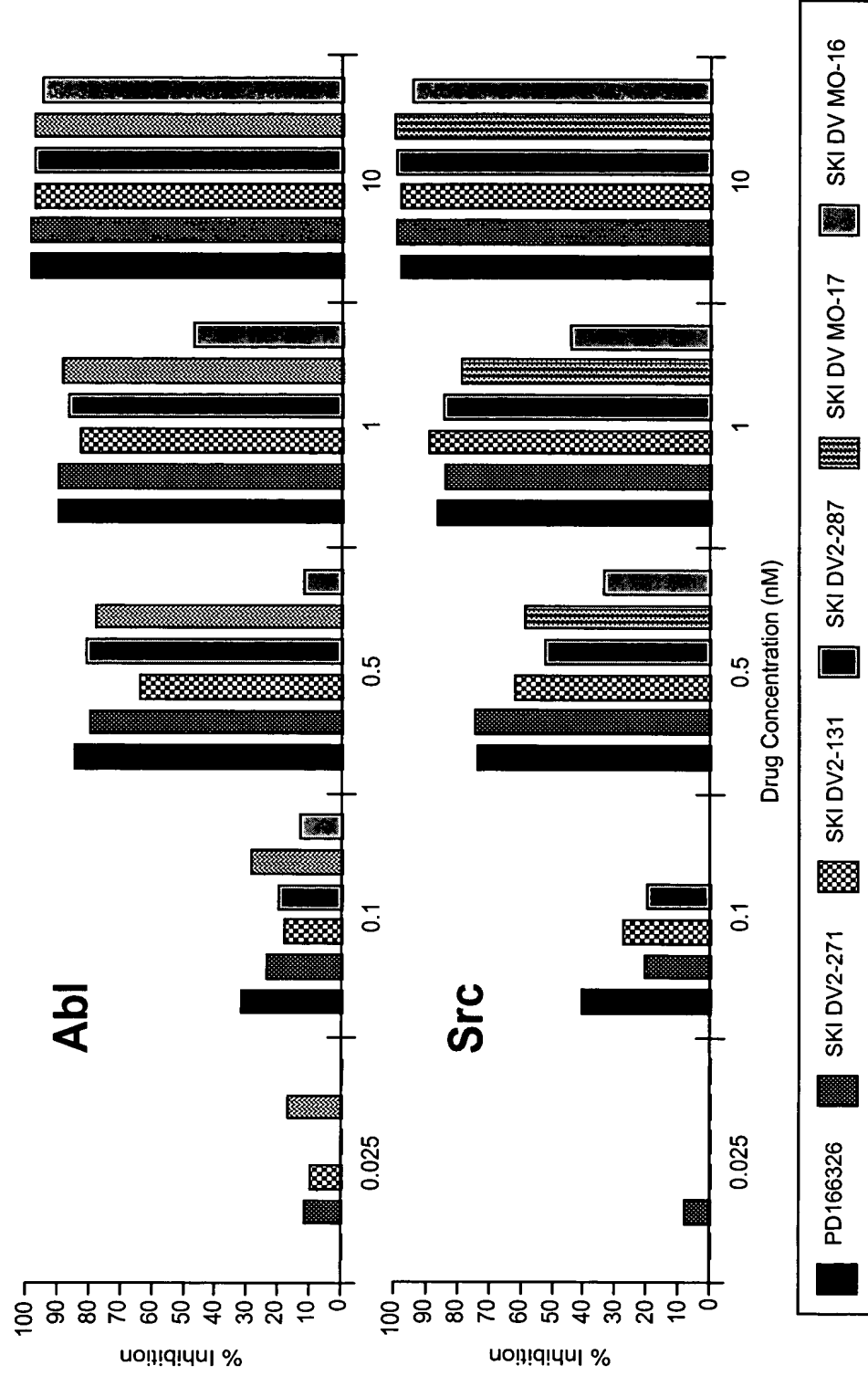
**Figure 28**



**Figure 29**

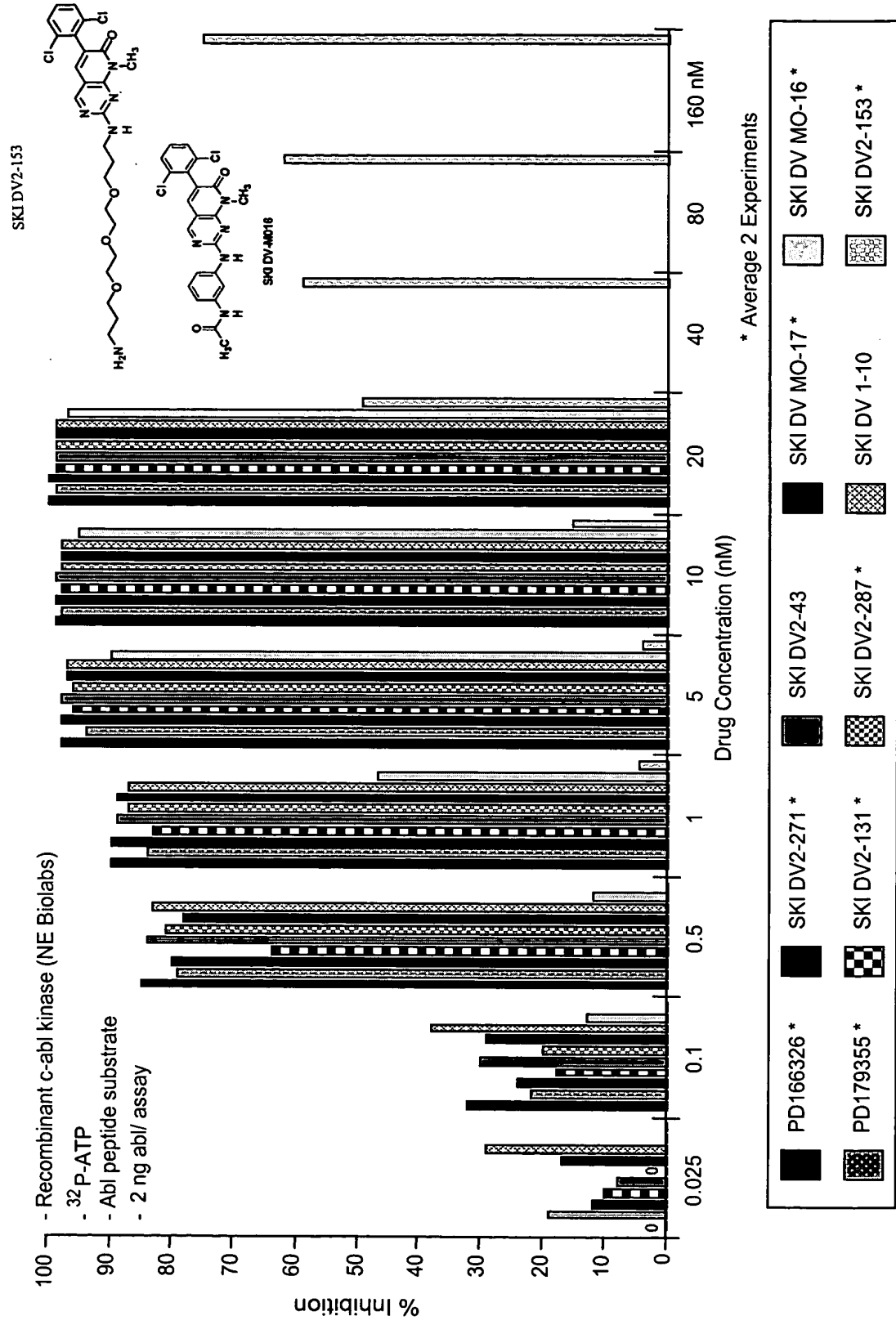


**Comparison of 6 of Most Inhibitory Pyrido- Pyrimidines to Bcr-Abl  
in Inhibiting Recombinant Abl & Src Kinases *in vitro***



**Figure 30**

***invitro* by 8 Pyrido- pyrimidine  
PD173955 & SKI DV2 153**



## Figure 31